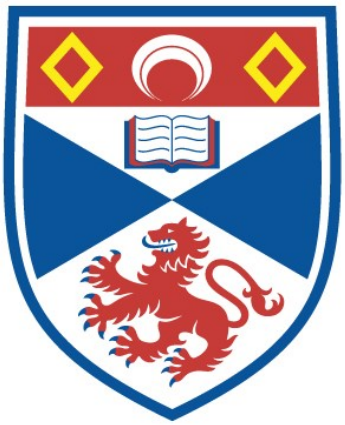
SOME STUDIES OF AROMATIC IODINATION AND DEIODINATION

Anthony Peter Sanderson

A Thesis Submitted for the Degree of PhD
at the
University of St Andrews



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OF

AROMATIC

IODINATION AND DEIODINATION

A Thesis

presented for the degree of

DOCTOR OF PHILOSOPHY

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by

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ABSTRACT

Kinetics of the iodination of a number of substituted benzenes and thiophens by iodine and nitric acid in acetic acid solution have been studied. The reaction is catalysed by dinitrogen tetroxide and hydrogen ions and evidence is presented to show that the iodinating species is protonated nitryl iodide, which reacts in a slow step with the substrate. Acidity function data for nitric acid in 10% aqueous acetic acid are presented and the charge-transfer complex formation between iodine and m-xylene in acetic acid has been studied.

The conversion of 4-iodoanisole into 2-iodo-4-nitroanisole by nitric acid has been shown to occur by rapid nitrodeiodination and iodination to give 2,4-di-iodoanisole and 4-nitroanisole, gradual nitrodeiodination of the former compound at the 4-position with the production of free iodine, and then very slow iodination of the latter compound at the 2-position. Nitrous acid and hydrogen ions act as catalysts and the preliminary step is thought to be nitrosodeiodination. The ortho:para ratio for the methoxy-group in nitrosodeiodination is very low. The ipso factors of Perrin and Skinner are discussed in the light of this and other work.

Transient intermediates observed in the nitrodeiodination reaction have been investigated using stopped-flow techniques and a water soluble substrate. These species are tentatively suggested to be σ-complexes.

The anomalously high rate of nitration of iodobenzene has been investigated and it has been found that this phenomenon is not due to a nitrodeiodination reaction, as had been suggested previously.

Work on the nitration of iodomesitylene has been investigated and it has been found that nitrosodeiodination is significant in this reaction, which is contrary to the findings of the previous workers.

A computer programme has been written to assist calculations on data obtained from radio-isotopic dilution experiments where two products are formed simultaneously from a single substrate. Another computer programme has been written to assist in the calculation of rate constants for reactions of the first and half order.

DECLARACTION

I declare that this thesis is based on the results of experiments carried out by me, that it is my own composition and has not previously been presented for a Higher Degree.

The work was carried out in the Department of Chemistry of the United College in the University of St. Andrews, under the direction of Dr. A.R. Butler, between October 1970 and June 1973.

CERTIFICATE

I hereby certify that Anthony Peter Sanderson has spent eleven terms at research work under my supervision, has fulfilled the conditions of Ordinance No. 12 (St. Andrews), and is qualified to submit the accompanying thesis in application for the degree of Doctor of Philosophy.

Director of Research

ACKNOWLEDGEMENTS

I would like to thank Dr. Anthony Butler for suggesting this topic of research and for his advice and encouragement which sustained the progress of the work.

My thanks go to the members of the Chemistry, Computational Science and Physics Departments who have given assistance and to Mrs. Pat Cooper for her careful typing of this thesis.

Finally, I gratefully acknowledge a studentship from the Science Research Council.

CONTENTS

PART I

INTRODUCTION

1. GENERAL

In 1896 Reverdin[1] published a paper in which he reported a study of the action of fuming nitric acid on 2- and 4-iodoanisole. Analysis of the main product of each of these reaction showed it to be 2-iodo-4-nitroanisole in both cases, and thus, in the case of 4-iodoanisole, an unexpected migration of the iodine from the 4- to the 2-position had taken place. This reaction was studied further by Robinson[2], who isolated 2,4-di-iodoanisole as an intermediate and proposed a mechanism for the rearrangement. However, some details were not clarified and so the work in this thesis was undertaken in an effort to elucidate the mechanism of the reaction further by means of kinetic and radiochemical labelling studies.

The use of nitric acid in this reaction brings to mind the iodination of aromatic compounds using the same reagent. Since an iodine atom migrates to a previously unsubstituted position during this reaction, it seemed likely that there is a connection between the migration reaction and aromatic iodination, particularly since, as Robinson[2] pointed out, the concentration of nitric acid is critical as to which reaction occurs.

Although aromatic bromination and chlorination have been studied extensively, aromatic iodination is little understood. Iodine does not react spontaneously with aromatic compounds, other than phenols[3,4] and amines[5], but iodination may be effected by the addition of an oxidising agent. The use of peracetic acid has been extensively investigated[6,7,8,9], but nitric acid, the reagent most commonly used in synthesis, does not seem to have been studied. The mechanism reported in most textbooks is erroneous, as was pointed out by Butler[10]. This mechanism proposes that the reaction is an equilibrium process,

$$ArH + I_2 \rightleftharpoons ArI + HI$$

in which the nitric acid acts to remove the small equilibrium quantities of hydrogen iodide, formed along with the aryl iodide by the action of iodine on the aromatic compound, thus causing the reaction to go to completion. There is, however, no evidence that iodination is an equilibrium reaction and, as Kekulé[11] noted, the necessary consequence of this mechanism being correct is that hydrogen iodide should react with iodobenzene to release iodine. It has been shown, however, that hydrogen iodide is not a sufficiently strong reducing agent to do this[12].

Since this mechanism is invalid it was decided to make first a study of aromatic iodination by iodine and nitric acid, the elucidation of the mechanism of this reaction giving insight into the iodine migration reaction.

It also seemed likely that for the iodine migration reaction concepts pertaining to aromatic nitrodeprotonation would be relevant, but this reaction has been so extensively investigated that it was felt that new work in this area would not be particularly fruitful. The work already carried out on aromatic nitration has been discussed both comprehensively[13,14] and recently[15] and it is not proposed to add to these reviews in this thesis, but rather to make use of well established ideas when relevant. It would seem of more use to review aromatic iodination and aromatic nitration where the displaced group is not hydrogen as a background to this work.

2. AROMATIC IODINATION

A. MOLECULAR IODINE WITHOUT A CATALYST

Bromine and chlorine are electrophilic enough to attack the benzene ring to give halobenzenes even in the absence of a catalyst. This is not the case with iodine and no chemical reaction occurs when iodine is mixed with an alkyl benzene. However it does react with such highly reactive nuclei as in phenols and amines, the former having been studied at varying pH's[3], but the reaction mechanism is complex and is not clearly understood and so these two substrates will not be considered further.

Strong[16] found evidence for the formation of an iodine-benzene complex after a mixture of the two had been subjected to flash photolysis, but actual substitution did not occur. Charge-transfer complexes have also been observed[17] for iodine and substituted benzenes.

B. USE OF AN OXIDISING AGENT AS CATALYST

Aromatic iodination is commonly effected by the addition of an oxidising agent to the reaction mixture. As stated previously, the generally reported role of these reagents is erroneous, but few such agents have been studied comprehensively enough for a reaction mechanism to have been proposed.

Probably the most often used oxidising agent used in synthetic aromatic iodination is nitric acid, and it is with this reagent that mechanistic studies and a proposed mochanism are described later in this thesis, such studies not having been reported previously.

Datta[18,19] iodinated an extensive range of aromatic nuclei, including benzene, toluene, the xylenes, mesitylene, ethylbenzene, halobenzenes and several carboxylic acids, by adding concentrated nitric acid slowly to a mixture of the aromatic compound and iodine and then refluxing for a time depending on how activated the

particular nucleus is.

Novikov[20] iodinated several alkylbenzenes in acetic acid using nitric acid and iodine, adding also some sulphuric acid which possibly indicates some form of acid catalysis in the reaction.

Varma[21] used nitrosulphonic acid, made by passing sulphur dioxide into fuming nitric acid, to iodinate a range of aromatic compounds and he later used sodium nitrite in sulphuric acid to iodinate benzoic acid and bromobenzene[22]. It is worth noting at this point that sodium nitrite is a source of the nitrogen oxides often present in nitric acid as impurities and this could be a clue to the effectiveness of this medium.

Possibly analogous with the above reactions is the preparation of iododurene by treatment of durene with sulphur iodide and nitric acid[23].

Extensive mechanistic studies have been carried out by Ogata and his co-workers on the use of peracetic acid as the oxidising agent in aromatic iodination. He originally found[6] that peracetic acid would effect the iodination of benzene and toluene and found that iodic acid was a side product of this reaction and the main product in the absence of an aromatic. Further studies[7] led him to propose acetyl hypoiodate or iodous acid as the attacking species, the formation of which being the rate determining step since the reaction was found to be zero order in aromatic. He found[7] that addition of sulphuric acid increased yields with benzene, iodobenzene and benzoic acid but decreased them with alkyl benzenes. Peroxybenzoic acid was found to be an unsatisfactory catalyst for iodination and it was concluded that the attacking species is acetyl hypoiodate. It was shown[8] that the reaction exhibits autocatalysis for compounds more activated than benzene and that

the reaction is catalysed by the addition of iodoaromatics. The autocatalysis is apparently due to the formation of aromatic iodoso-compounds or aryl iodine diacetates which have been shown to catalyse the reaction, which Ogata concluded to be electrophilic by the orientation and activation of attack. He also found[24] that the same species, acetyl hypoiodate, is responsible when aromatic compounds are iodinated by peracetic acid and alkyl iodides, yielding alkyl acetates as well as the iodinated compound. It was found that secondary alkyl iodides were more effective for iodination than primary, and the acetyl hypoiodate formed in this reaction will add across the double bond of cyclohexene[25].

Iodic acid has been used with iodine by several workers to iodinate aromatic rings. It was found[26] that iodobenzene can be made in 83% yield by the reaction of iodine and iodic acid in 90% aqueous acetic acid with benzene at 90°, but iodic acid alone will not effect this iodination.

Semin'ko[27] reported that iodic acid, iodine and sulphuric acid form compounds of variable composition which have strong iodinating properties. He varied the ratio of iodic acid: iodine and found the most effective ratio is one of 4:3 which he ascribed to $I_2O_3H_2SO_4$ and $I_2O_4H_2SO_4$.

Arotsky[28] found that a molar ratio of 7:1 of iodine: potassium iodate in sulphuric acid gives the tri-iodide cation which reacts with a wide range of aromatic compounds except the most deactivated. This mixture was used by Masson[29], and is often referred to as Masson's reagent, who suggested that the iodinating species was $(I_{2n+1})^+$. Arotsky proposed I_3^+ as the species and in further studies[30] found an isotope effect of 2, correlated the rate constants with the Brown and Okamoto σ^+ constant and has studied

solvent effects on the reaction.

Jurd[31,32] used hydrogen peroxide with iodine to iodinate tyrosine and its derivatives, anisole and naphthol ethers, and mercuric oxide as catalyst to iodinate aromatic ethers and 2-naphthol. The former reagent has also been used by Kumler[33] to iodinate several aromatic compounds and the latter by Hoch[34] to iodinate anisole. No mechanistic studies on these two reagents appear to have been carried out.

Elbs[35] found that aromatic compounds are readily iodinated by iodine and sodium persulphate and even higher yields are obtained if ammonium persulphate is used[36]. Cupric chloride, silver sulphate and sodium acetate also act as catalysts for the reaction.

Sulphur trioxide[37] has been used to iodinate deactivated substrates such as phthalic anhydride, and Suzuki[38] examined the iodination of aromatic compounds with bulky groups using silver perchlorate, hydrogen peroxide, iodic acid, potassium persulphate and others, but found that the best catalyst was periodic acid dihydrate.

C. USE OF IODINE MONOCHLORIDE

Iodine monochloride is an iodinating species in its own right. Berliner[39] proposed H_2OI^+ as the active species in water and later[40] used the method to prepare iodo-compounds from such activated compounds as anisole.

Andrews and Keefer[41] carried out some mechanistic studies on this reagent in acetic acid and found that the reaction is first order in aromatic and second order with respect to halogen, but the reaction tends to first order in both as the temperature is raised. This pattern resembles that in molecular bromination and suggests

that the attacking species is iodine monochloride, which at lower temperatures can assist the breaking of the iodine-chlorine bond, while at higher temperatures heterolysis occurs spontaneously. When zinc chloride is added[41] the reaction is first order in aromatic, iodine monochloride, and the added catalyst, indicating that zinc chloride also assists heterolysis of the I-Cl bond. In trifluoro-acetic acid the reaction is first order in aromatic and iodine monochloride, either because the solvent acts as assisting group or because the polarity is sufficient for spontaneous heterolysis. In carbon tetrachloride the reaction is third order in iodine monochloride[42] indicating that two molecules are needed to assist the breaking of the iodine-chlorine bond and in hydrochloric acid iodine monochloride is considered to act via a positive species[39].

D. USE OF SILVER SALTS AS CATALYSTS

Barker and Waters[43] iodinated several aromatic compounds and cyclohexane in sulphuric acid with iodine and silver sulphate. Hazeldine and Sharpe[44] found that silver trifluoroacetate and iodine in nitromethane gave a powerful iodinating agent which iodinates aromatic compounds, having the same properties as an electrophile and which, they concluded, was either trifluoroacetyl hypoiodate or silver iodide di-trifluoroacetate. They could find no evidence for the $(ClO_4)_x$ species, postulated earlier by Gomberg[45], resulting from the reactions of silver perchlorate and iodine. Earlier workers[46] also found no evidence for this species in work which demonstrated that silver perchlorate and iodine do not react with chloroform, hexane or cyclohexane but iodinate benzene and chlorobenzene readily and toluene and nitrobenzene slowly. These reactivities suggest that the reaction is not electrophilic unless another factor accounts for the low reactivity of toluene. They postulated the species

$IClO_4$ as being responsible for this reaction.

Hassner, Kropp, and Kent[47] reported that nitryl iodide is the iodinating species formed from silver nitrite and iodine. It was identified because it added across an olefinic double bond.

E. INDIRECT IODINATION

Aromatic iodides may be prepared by two or more step reactions, in which a group is introduced into the nucleus and then displaced by an iodine atom. Probably the best known of these reactions is diazotization. Many iodoaromatics have been made in high yield by reacting the diazonium salt in aqueous solution with potassium iodide, the mixture then being heated until nitrogen evolution has ceased. One example of this is the preparation of iodobenzene in 70% yield starting from aniline[48].

Iodination of aromatic nuclei has also been effected by first introducing a -HgCl group and displacing it with molecular iodine: 4-iodobenzoic acid[49] is an example of a compound synthesised in this manner.

Within the past few years the use of thallium in preparative organic chemistry has been developed greatly by McKillop, Edwards and their coworkers. These reactions are simple, give good yields, and exhibit high positional selectivity[50] and include a novel method of iodination[51,52].

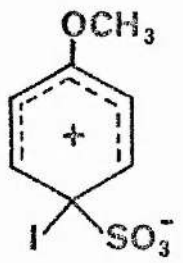
Arylthallium ditrifluoroacetates, prepared by the action of thallium trifluoroacetate on the aromatic compound in trifluoroacetic acid, react rapidly with aqueous potassium iodide to give thallium iodide and the corresponding aromatic iodide. By slightly varying methods all but the most activated aromatic compounds can be iodinated in this way. With such compounds as biphenyl and naphthalene competitive oxidation reactions decompose the substrates: however,

such compounds can be iodinated using molecular iodine and utilising thallium trifluoroacetate as an oxidant. Thallation is almost certainly the most effective method of iodination, the only drawbacks being the toxicity of thallium and the relatively high cost of thallium compounds compared with other iodinating agents.

Iodobenzene has also been prepared[53] by the action of molecular iodine on the Grignard reagent formed from bromobenzene.

F. MISCELLANEOUS

Suzuki[54] has developed a method of iodination based on the long known migration in the presence of sulphuric acid of iodine atoms in the nucleus of aromatic iodocompounds (the Jacobsen reaction[55]). A variety of polyiodo compounds have been prepared from, readily available, simpler iodocompounds. This method is particularly applicable to the preparation of symmetrically substituted or fully iodinated compounds, and about forty polyiodocompounds have been described. In later work[56] he proposed a mechanism for the reaction starting with 4-iodoanisole, postulating as an intermediate a brown complex to which he assigned the structure:



A reaction using one mole of morpholine to three moles of iodine has been shown[57] to give high yields of iodoaromatics by the postulated intermediacy of the species $(OCH_2)_2NI.HI$, and this reagent was found to be very effec tive for iodinating benzofuran.

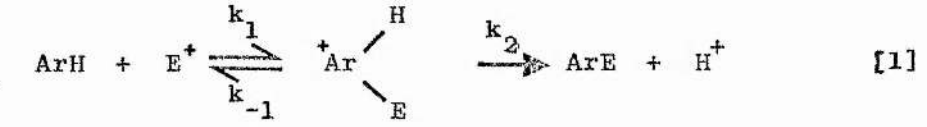
Organic iodination has been reviewed by Roedig[58], this review covers aliphatic as well as aromatic iodination.

3. AROMATIC NITRATION INVOLVING DISPLACEMENT OF GROUPS OTHER THAN HYDROGEN

A large class of aromatic substitution reactions is that in which a substituent, X, in an aromatic compound, is replaced by an electrophilic reagent, Y, since X and Y can each be one of a large number of groups. The reactions most usually discussed are those in which X is hydrogen, but this discussion concerns reactions where Y is a nitrating agent and X is not hydrogen. In these reactions care is necessary to ensure that the reaction is replacement of the substituent by a nitro-group rather than replacement by hydrogen followed by normal nitration.

A. NITRODEDEUTERIATION AND DETRITIATION

The question of whether electrophilic aromatic substitution is a two-step process proceeding by an intermediate;



[1]

or a one-step process;

$$ArH + E \longrightarrow \text{Transition State} \longrightarrow ArE + H^+ \qquad [2]$$

has been investigated extensively using deuteriated and tritiated aromatic compounds. The nitrations of benzene[59], toluene[60], bromobenzene[60], naphthalene[60] and nitro benzene[59,61] were found to exhibit no isotope effects when the rates for normal and labelled compounds were compared. These results are consistent with mechanism [1] where the slow step is attack by the electrophile (i.e. k_1). However, as pointed out by Hammond[62], such results alone do not rigorously exclude the one step mechanism. It can be concluded from this evidence, in isolation, only that the stretching of the

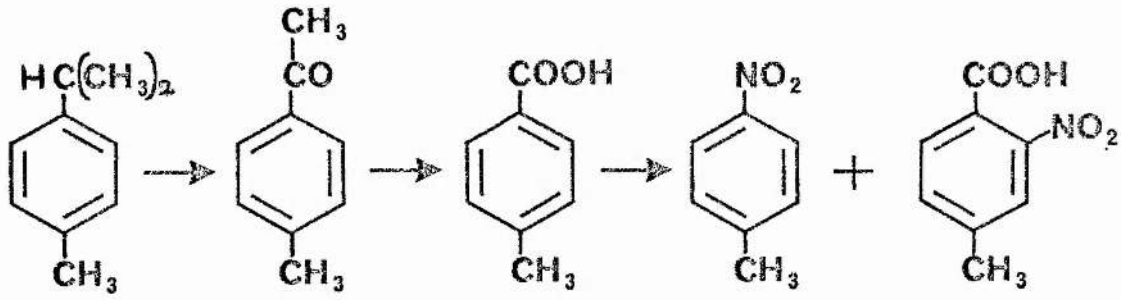
carbon-hydrogen bond has not made much progress in the transition state of the slow step.

B. NITRODEALKYLATION

When certain alkylbenzenes are nitrated, nitrodealkylation occurs as a side-reaction. This process has not been observed in the nitration of monoalkyl benzenes but only in the polyalkyl derivatives suggesting that the reaction is electrophilic.

When p-cymene is nitrated, as well as 2-nitrocymene, 4-nitrotoluene is a major product[63]. Since the isopropyl group is readily oxidised it is not surprising that methyl-p-tolyl ketone, p-toluic acid and 2-nitro-p-toluic acid have also been reported[63] as side products of this reaction.

It was suggested[64], to explain the formation of both oxidation and side products, that the following series of reaction take place;



If this were correct, then, either methyl p-tolyl ketone or p-toluic acid, should yield some 4-nitrotoluene among its nitration products. It was found[65] that nitration of methyl-p-tolylketone with fuming nitric acid and sulphuric acid at -10° gave methyl-2-nitro-p-tolyl ketone, while, at 70°, the principal product was 2,6-dinitro-p-toluic acid. The product from p-toluic acid was either 2-nitro- or 2,6-dinitro-toluic acid, but no replacement product was obtained even under drastic conditions, indicating that the suggested mechanism is incorrect.

Replacement of an isopropyl group also takes place with 1,4-di- and 1,2,4,5-tetra-isopropylbenzene, while nitration proceeds normally with 1,3-di-, 1,2,4-tri- and 1,3,5-tri-isopropylbenzene[66]. In the case of 1,4-di-isopropylbenzene[66] the effect of the composition of the nitrating mixture is notable. The products from the nitration by nitric acid and acetic anhydride and by nitric acid and sulphuric acid were a mixture of replacement and normal nitration products in both cases, but, in the former case the ratio of replacement products to straight nitration products was found to be 1.44:1, while in the latter it was 4.74:1. When 1,2,4,5-tetra-isopropyl-benzene[66] was reacted with nitric acid and acetic anhydride at 47°, 80% of the product was formed by the replacement reaction, while at 80° all the product is formed by this route, illustrating the effect of temperature on the reaction.

The product from nitration of 5-amino-1,2,4-tri-isopropylbenzene in 98% sulphuric acid[66] is 6-nitro-4-amino-1,3-di-isopropyl benzene which is also obtained by the nitration of 4-amino-1,3-di-isopropyl-benzene.

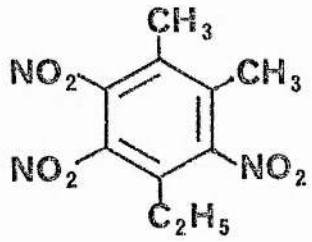
Trinitro-m-xylene is obtained under nitrating conditions from both 1,3-dimethyl-5-t-butylbenzene[67] and 3,5-dimethyl-t-amylbenzene[67], the latter giving the higher yield. More examples closely related to these have been studied[68,69].

When alkylbenzenes more alkylated than tri-alkylbenzenes, and some of their derivatives are nitrated, the conditions can be adjusted to give normal nitration or replacement of one or more alkyl groups by a nitro group.

Nitration of pentamethyl-, penta-ethyl-, hexamethyl- or hexa-ethylbenzene gives dinitroprehnitene with the methyl derivatives[70,71], and 1,4-dinitro-tetra-ethylbenzene with the ethyl derivatives[72,73,74].

The nitrating agent can be either fuming nitric acid, alone or with sulphuric acid in chloroform. Higher yields are obtained in the cases of the pentasubstituted compounds.

Ethylmesitylene, when nitrated with fuming nitric acid and sulphuric acid, undergoes an apparent migration of one methyl group and one methyl group is displaced[75] to give;



Nitrodealkylation has been recorded with thymol, thymol ethers and related compounds[68,69,76,77,78,79] and is often encountered in the literature in connection with the search for musk substitutes.

It may be concluded from these references that certain conditions facilitate the removal of an alkyl group in aromatic nitration. Since the alkyl group is displaced without its bonding electron pair, the stability provided by the more branched carbonium ion might be presumed a necessary condition for such a reaction to occur, except under very severe conditions. It is to be expected, therefore, that the ease of removal of alkyl groups will vary in the order of their stabilities as cations, that is, tertiary > secondary > primary.

A second condition favouring displacement of alkyl groups is activation of the position from which the group is displaced by an electron releasing substituent, in the 2- and 4-positions. In addition steric acceleration is undoubtedly an important driving force in highly congested systems.

The displaced alkyl group would be expected to appear in the

products as an olefin, possibly rearranged, as an alcohol, or as an ester. Another possibility is that migration of the alkyl group to another position in the benzenoid ring occurs.

C. NITRODEACYLATION

Some polyphenolic aldehydes and ketones and their ethers are known to undergo displacement of formyl or acyl groups under aromatic nitrating conditions. For example, methyl-3,4,5-trimethoxyphenyl ketone gives 1,3,5-trimethoxy-5-nitrobenzene and acetic acid when reacted with nitric acid[80]. When nitrated, 4-methoxybenzaldehyde[81] gives about 30% 5-nitroanisole, similarly methylene-di-oxybenzaldehyde[82] undergoes replacement of the formyl group during nitration and piperonal and vanillin behave similarly.

Further examples of deacylation are observed when a nitrating mixture is reacted with 3,4-dimethoxyacetophenone[83] to give 1,2-dimethoxy-4,5-dinitrobenzene; 2,6-dibromo-4-aminobenzophenone[84] and 2,6-dibromo-4-aminoacetophenone[84] both give 2,6-dibromo-4-nitronitramine; 3,4,5-trimethoxyacetophenone gives 3,4,5-trimethyl-nitrobenzene[83].

D. NITRODECARBOXYLATION

Nitrodecarboxylation reactions sometimes accompany the nitration of polyalkyl benzoic acids: for example, nitration of prehnitene carboxylic acid gives dinitroprehnitene[85]. Nitration of amino, hydroxy, and alkoxy-benzoic acids is also often accompanied by this displacement reaction. In general the carboxyl group is more readily replaced when there are two or more ortho/para directing groups in the aromatic nucleus.

Salicylic acid, on nitration, gives picric acid[86] and anisic acid gives nitroanisole, 2,4-dinitroanisole, or 2,4,6-trinitroanisole,

along with the normal nitration products, depending on the severity of the nitrating conditions[86]. Nitration of o-nitrosalicylic acid gives dinitrophenol[87] and dichlorosalicylic acid gives di-chloro-nitrophenol[88]. β-Resorcylic acid has been nitrated[89] to yield styphnic acid, veratric acid to give 4-nitroveratrole[90], and hemipinic acid to give nitro-dimethoxybenzoic acid[91].

The nitration of p-dimethylaminobenzoic acid[92] can lead to a variety of products depending on the composition of the nitrating mixture and a complicated mixture of replacement products results. This substrate will also react with hydrochloric acid and sodium nitrite to displace the carboxylic acid group by a nitro group[93].

E. NITRODESULPHONATION

It is well known that displacement of the sulphonic acid group often occurs during nitration of aromatic sulphonic acids, with or without the normal products of hydrogen expulsion depending on the reaction conditions and the nature of the organic substrate. Kinetic studies of this reaction have not been reported, but, in general, aromatic protons are replaced before nitrodesulphonation occurs.

One well known example of this type of reaction is the preparation of picric acid[94] from phenol by sulphonation followed by nitration.

Nitrodesulphonation reactions have been reviewed in detail by Suter[95].

F. NITRODESILYLATION AND NITRODESTANNATION

The cleavage of aryl-silicon bonds by nitrating reagents was first reported by Kipping[96]. Studies of this reaction are complicated by concurrent protodesilylation which occurs in strongly

acidic media. To avoid this complication copper nitrate in acetic anhydride has been used as the nitrating agent in an investigation[97] of the nitrodeprotonation and nitrodesilylation of various isomeric tolyltrimethylsilanes. These studies showed that the maximum amount of the latter reaction which occurred was only about 25%, indicating that it occurs less readily than protodesilylation. This conclusion was born out by the results obtained from the competitive nitration of benzene and trimethylsilylbenzene[98].

More recently, it has been found[99] that nitrosyl chloride will displace trimethylsilyl groups in the presence of a catalyst, and trimethylstannyl groups with no catalyst.

With nitric acid and acetic anhydride as the nitrating agent[100], desilylation predominates and p-bistrimethylsilylbenzene gives trimethyl-p-nitrophenylsilane in 80% yield. This nitrating agent was found[101] to desilylate a range of trimethylsilanes either with no other substituent in the benzenoid ring or a methyl- or chloro-group in the 3- or 4-position, and it is suspected that this reaction occurs via nitrosodesilylation.

G. DISPLACEMENT OF ARYLAZO GROUPS BY NITRO GROUPS

The arylazo group ArN=N- can exist as a positive ion and should therefore be susceptible to displacement from an aromatic nucleus by electrophilic reagents. The formation of 2,4-dinitrophenol through the nitration of azo-phenol[102] may proceed by such a path.

H. NITRODEHALOGENATION

It is sometimes observed that halogenated phenols or phenolic ethers, where the halogen atom is located ortho or para to a hydroxy, alkoxy or aryloxy group, undergo replacement of the halogen when nitrated. In some cases the free halogen, released in the displacement,

itself re-enters the aromatic ring, thus, giving rise to apparent substitution with rearrangement. It is one such reaction that is examined in detail later in this thesis, that is the action of nitric acid on 4-iodoanisole[1], the main product being 2-iodo-4-nitroanisole. No previous mechanistic study of the nitrodehalogenation reaction has been reported, except that of Robinson[2] also on the above reaction, but, it is known that the ease with which the halogens are displaced from the aromatic nucleus is iodine > bromine > chlorine.

Examples of nitrodehalogenation reactions in the literature are numerous, and some are presented in Table 1.

In this table example 1 illustrates displacement of a chlorine atom, the rarest of these dehalogenation reactions and in this example surprisingly mild conditions are needed to effect this reaction. Examples 2-9 illustrate displacement of bromine, a more common occurence during nitration, example 3 showing that a bromine para to the hydroxyl group is displaced before those ortho to it. Example 8 illustrates the simultaneous processes of oxidation of a nitroso group and displacement of bromine by the same reagent, nitric acid, example 7 illustrates activation by an aryloxy group, and example 4 illustrates activation by an ethoxy group, in contrast to the usual activating groups, methoxy and hydroxy. Example 9 shows that it is not only benzene nuclei that are involved in these type of reaction, but, in this case the reaction occurs with a thiophen nucleus.

Examples 10-14 illustrate the displacement of the most easily removed halogen, iodine. Example 13 is unusual in that no hydroxyl alkoxyl or aryloxyl group is present, but the influence of the three methyl groups is sufficient for this reaction to occur, and example 14 shows that iodine is replaced more readily than

TABLE 1

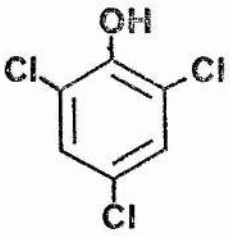
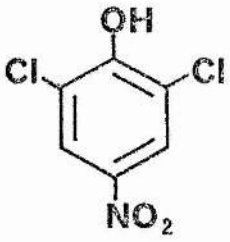
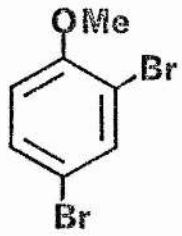
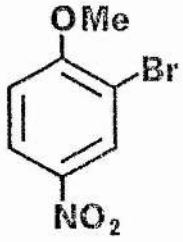
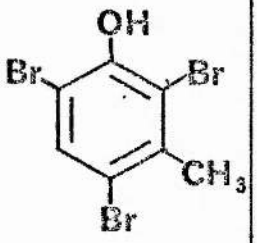
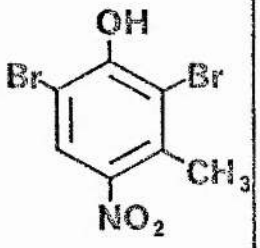
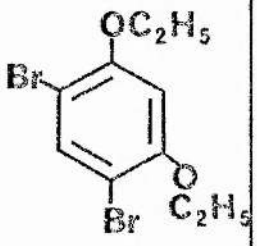
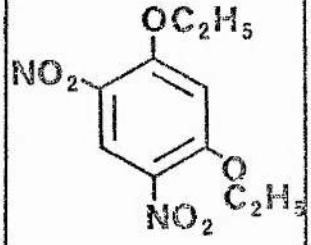
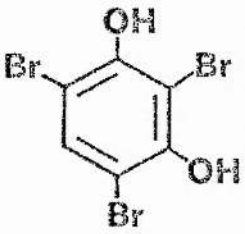
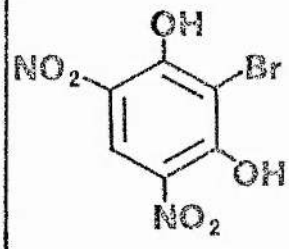
e.g.	Substrate	Nitrating agent	Product	Ref.
1		$NaNO_2$/AcOH		103
2		HNO_3		104
3		HNO_3/AcOH		105
4		fuming HNO_3		106
5		fuming HNO_3		106

TABLE 1 (cont.)

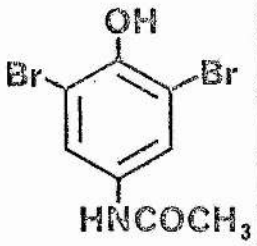
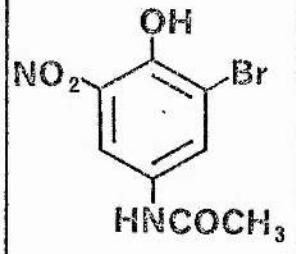
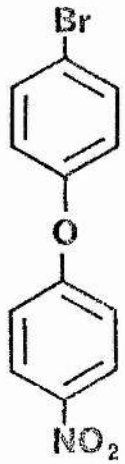
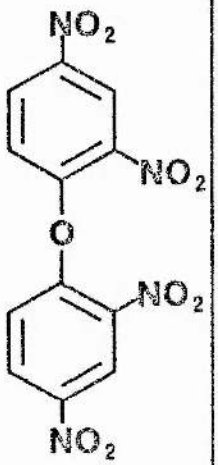
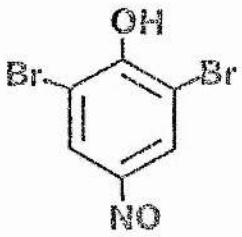
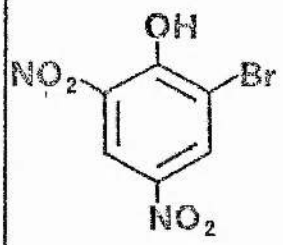
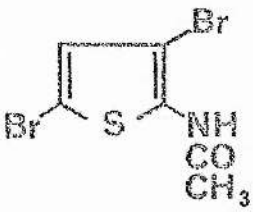
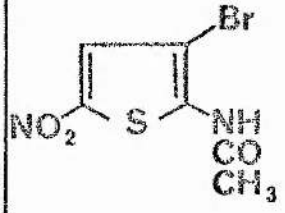
e.g.	Substrate	Nitrating agent	Product	Ref.
6		HNO_3		107
7		HNO_3		108
8		HNO_3		109
9		N_2O_3		110

TABLE 1 (cont.)

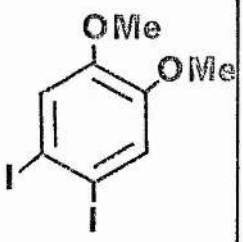
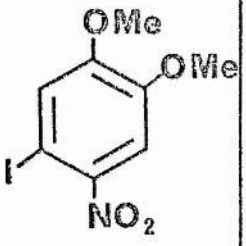
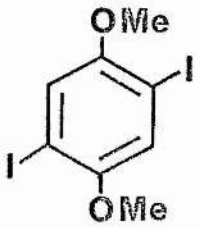
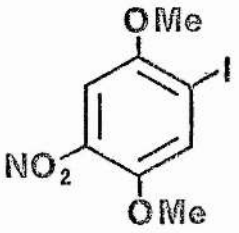
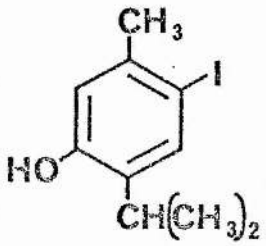
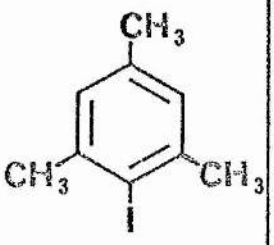
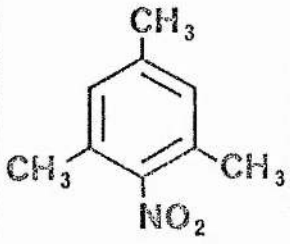
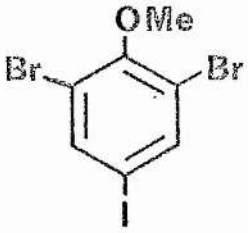
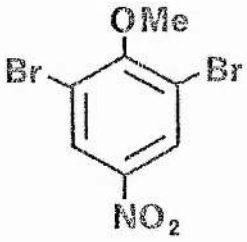
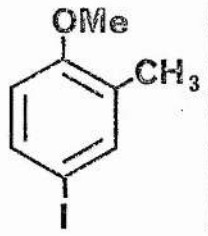
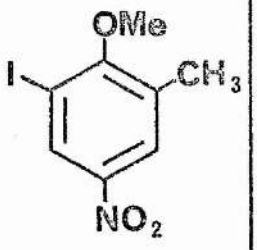
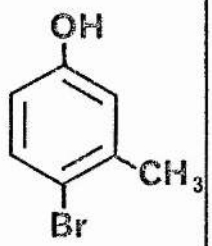
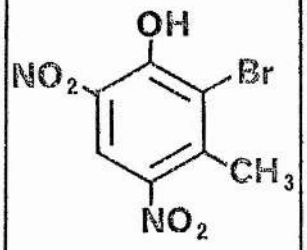
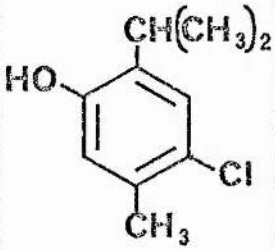
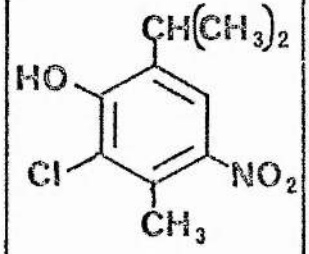
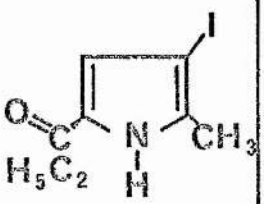
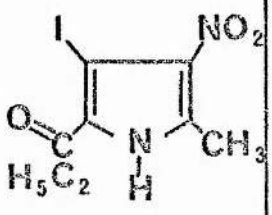
e.g.	Substrate	Nitrating agent	Product	Ref.
10		HNO_3/AcOH		2
11		HNO_3/AcOH		2
12		HNO_3/AcOH	A mixture of nitrothymols	111
13		HNO_3		112
14		fuming HNO_3		113

TABLE 1 (cont.)

e.g.	Substrate	Nitrating agent	Product	Ref.
15		HNO_3		2
16		HNO_3		114
17		HNO_3/AcOH		115
18		HNO_3 at 0^o		116
19		H_2SO_4/HNO_3		117

bromine, although it must be taken into consideration that the iodine atom is in the more favourable 4-position.

Examples 15-18 illustrate displacement of iodine, bromine, and chlorine by a nitro group with migration of the halogen to another position in the aromatic ring. Example 18 shows this type of reaction occurring with a pyrrole nucleus rather than a benzene nucleus.

Example 19 is singular in that the substrate is deactivated towards electrophilic attack. Schofield and coworkers[117] have studies this reaction and claim that the attacking species is the nitronium ion.

In all the examples in the table, the displacement reaction is not the only one that occurs, normal nitration can occur simultaneously, but nitrodehalogenation does count for a substantial proportion of reaction.

PART II

RESULTS AND DISCUSSION

1. MECHANISM OF THE IODINATION OF SUBSTITUTED BENZENES AND THIOPHENS

In the normal synthetic procedure for the preparation of iodobenzene, a mixture of iodine, benzene, and concentrated nitric acid is heated under reflux[18]. Such vigorous conditions are unsuitable for a mechanistic study and, bearing in mind the example of Ingold's work on aromatic nitration[118], it was decided to use acetic acid as solvent. Iodine dissolves in glacial acetic acid[119] containing 10% nitric acid and exists largely as the diatomic molecule[120]. On addition of toluene to such a solution, the brown colour, due to iodine, disappears, indicating that the conditions are suitable for a kinetic investigation of the reaction.

According to Datta and Chatterjee[18] the product of this reaction should be a mixture of 2- and 4-iodotoluene, but the iodine concentration in acetic acid solution is too low (10^{-3} M) to permit separation and indentification of the products. However, by carrying out the reaction with [^{14}C]-toluene and dilution of the products with inactive samples of 2- and 4-iodotoluene, it was shown, by radioactive counting, that these isomers are the products of the reaction under kinetic conditions, but the isomer ratio was not determined due to experimental difficulties. It was also shown, from this experiment, that iodine was quantitatively converted into iodotoluene, unlike the situation in chlorination and bromination where only half the halogen becomes attached to the aromatic ring. This has been confirmed by quantitative separation of the products of the iodination of m-xylene under preparative conditions[121].

Under kinetic conditions, the brown colour due to iodine disappears much more rapidly upon addition of mesitylene than xylene, with toluene the reaction is incomplete after several hours and with benzene it is incomplete after many days. This trend is

also observed in the iodination of thiophens where 2-phenylthiophen reacts faster than thiophen which, in turn, reacts faster than 2-chlorothiophen. From this evidence it was concluded that the iodinating species is electrophilic.

The kinetics of the reaction were studied by monitoring the disappearance of the absorption due to iodine or, more probably, a complex of iodine and acetic acid[122] at 475 nm, generally with use of m-xylene as substrate. A plot of optical density against time was found to be sigmoid, characteristic of an autocatalytic reaction. By analogy with aromatic nitration, nitrous acid immediately suggested itself as the species responsible[123] and addition of dinitrogen tetroxide (the form in which nitrous acid exists in the presence of nitric acid) was found to remove the sigmoid character of the plot and to catalyse the reaction. Also, addition of urea, which destroys nitrous acid, was found to drastically reduce the rate of reaction. In most experiments it was found to be more convenient to add aqueous sodium nitrite than dinitrogen tetroxide, in order that concentrations might be more easily estimated, following the procedure of Ogata and Tezuka[124], and so the reaction medium was normally 10% (v/v) aqueous acetic acid.

The rate of reaction, in the presence of an excess of nitric acid, sodium nitrite and the substrate, was found to be proportional to the square root of the iodine concentration, suggesting, since under these conditions iodine exists as a diatomic molecule, that the iodinating species contains only one atom of iodine. Integration of this rate equation is given in Appendix 3 and values of the observed constant, k(obs.), were obtained by plotting $[I_2]^{\frac{1}{2}}$ against time, the plots being linear over at least three half-lives. The molar extinction coefficient for iodine under these conditions was found

to be 769.

There are three variables in the reaction mixture, sodium nitrite, nitric acid, and the substrate, and determination of how the rate of reaction depended upon each produced a number of unexpected and puzzling results.

Sodium nitrite.

Sufficient sodium nitrite was added to make the reaction non-autocatalytic and the lower limit was found to be 0.005 M (with $[I_2]_o$ = ca. 0.001 M). Increasing the nitrite concentration affected the rate in the manner shown in Figure 1 (see Table 2). A similar result was obtained by Ogata and his co-workers[125] in a study of the oxidation of benzyl ethers and diphenylmethane by nitric acid in acetic acid. They concluded that the limit of solubility of dinitrogen tetroxide was reached at about 0.02 M-sodium nitrite. Thus, because of experiment difficulties, it is impossible to study the dependence of rate on sodium nitrite concentration over a sufficiently large range for any definite conclusion to emerge.

A study of the spectrum of sodium nitrite in nitric acid, in acetic acid showed that the nitrite is quantitatively converted into dinitrogen tetroxide[126], and it has been assumed that this is the species responsible for catalysing aromatic iodination.

Nitric acid

Keeping the concentrations of sodium nitrite and aromatic compounds constant and increasing the amount of nitric acid present led to a substantial increase in rate. There was found to be a linear relationship between k(obs.) and $[HNO_3]^2$ but this was thought to be possibly fortuitous as some acidity function data for

TABLE 2

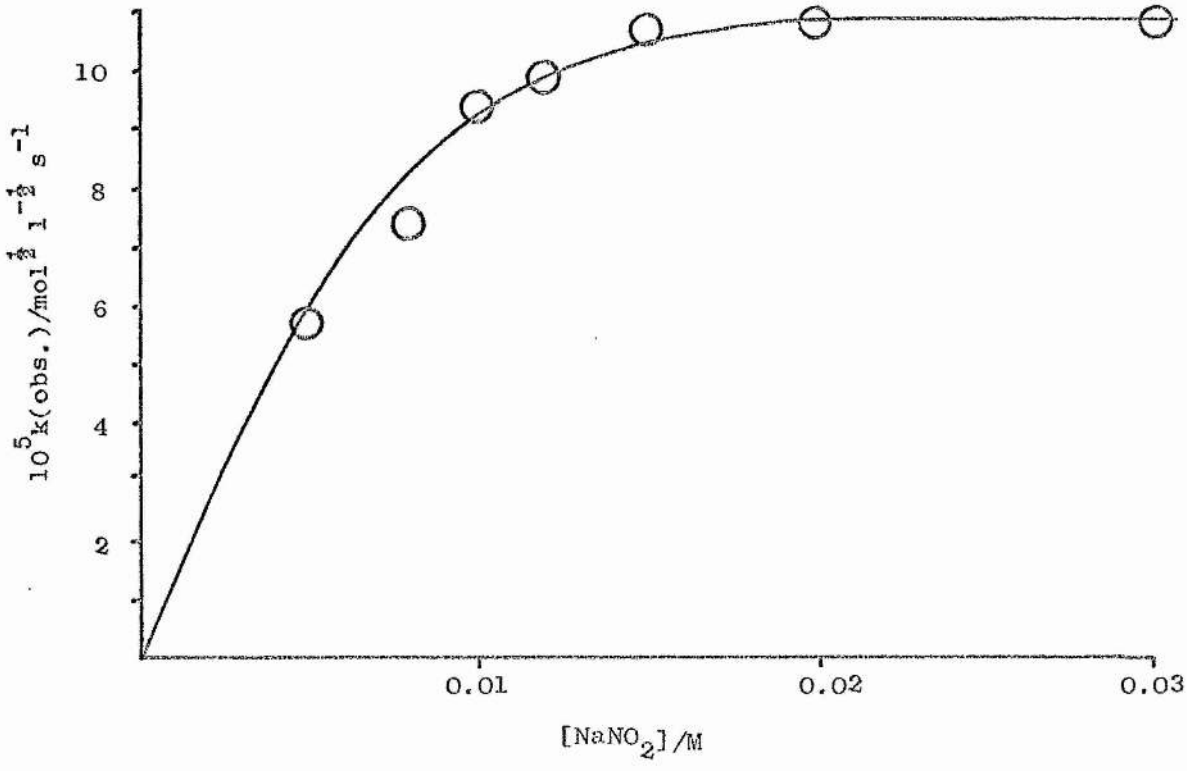
Effect of nitrite on the rate of iodination of m-xylene in acetic acid

$[I_2]_o = 1.25 \times 10^{-3}$ M $[HNO_3] = 1.56$ M

[m-xylene] = 0.042 M Temperature 25°

$[NaNO_2]$/M	10^5 k(obs.)/mol$^{\frac{1}{2}}$ l$^{-\frac{1}{2}}$ s^{-1}
0.005	5.7
0.008	7.4
0.010	9.4
0.012	9.9
0.015	10.7
0.020	10.8
0.030	10.8

Figure 1. Effect of nitrite on the rate of iodination of m-xylene.



for hydrochloric acid in aqueous acetic acid[127] suggested that $[HNO_3]^2$ might be a measure of the h_o value. No values of h_o for nitric acid in 10% aqueous acetic acid were available and so these were determined for the relevant range of nitric acid concentrations. A plot of k(obs.) against h_o for m-xylene, see Figure 2 (Table 3), is linear and it was concluded that the probable role of nitric acid in aromatic iodination is simply that of an acid, and that the iodinating species is formed by the protonation of some species resulting from the reaction of iodine and dinitrogen tetroxide. This idea was confirmed since dinitrogen tetroxide and iodine in glacial acetic acid do not react with m-xylene but, on addition of perchloric acid, there is rapid disappearance of the iodine. Similar catalysis by acid has been reported[26] for aromatic iodination in acetic acid in the presence of iodic acid.

Substrate

The variation of rate with the concentration of substrate proved to be the most puzzling feature of this reaction. Typical results for m-xylene, at three different nitric acid concentrations, are shown in Figure 3 (see Table 4). These results and similar ones for mesitylene (Figure 5, Table 6), 2-bromoanisole (Figure 4, Table 5), thiophen (Figure 6, Table 7) and 2-chlorothiophen (Figure 7, Table 8), show a very exact linear relationship between k(obs.) and the square-root of the concentration of substrate, typical plots of this type for m-xylene are shown in Figure 8 (Table 4). It was difficult to decide whether this result was meaningful or fortuitous. It is possible to accommodate such a result into a reaction scheme if either iodine or dinitrogen tetroxide is removed by complexing

TABLE 3

Variation of rate of iodination of m-xylene with acidity

$[I_2]_o = 1.21 \times 10^{-3}$ M $[NaNO_2] = 0.005$ M

[m-xylene] = 0.080 M Temperature 25°

$[HNO_3]$ M = 0.080 M	h_o	10^4 k(obs.)/$mol^{\frac{1}{2}}$ $l^{-\frac{1}{2}}$ s^{-1}
0.48	1.08	0.20
0.81	2.00	0.42
1.13	3.20	0.79
1.29	4.03	1.05
1.45	5.01	1.20
1.61	6.17	1.49

$[I_2]_o = 1.15 \times 10^{-3}$ M $[NaNO_2] = 0.005$ M

[m-xylene] = 0.82 M Temperature 25°

$[HNO_3]$/M	h_o	10^4 k(obs.)/$mol^{\frac{1}{2}}$ $l^{-\frac{1}{2}}$ s^{-1}
0.32	0.60	0.36
0.81	2.00	1.14
1.13	3.20	2.18
1.45	5.01	3.73
1.61	6.17	4.53

Figure 2. Variation of rate of iodination of m-xylene with acidity.

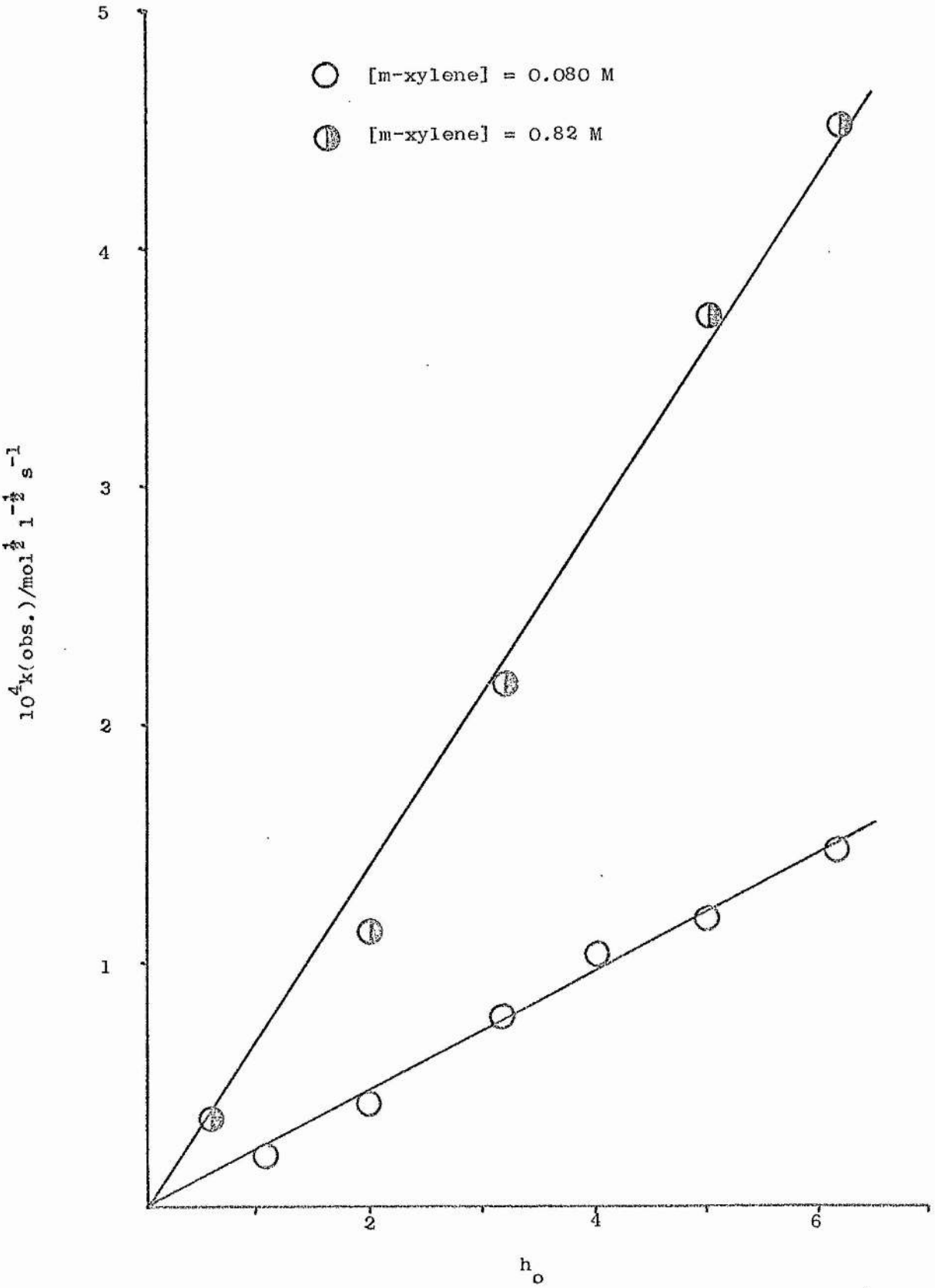


TABLE 4

Effect of m-xylene concentration on the rate of iodination at various acidities

$[I_2]_o = 1.24 \times 10^{-3}$ M $[NaNO_2] = 0.005$ M

$[HNO_3] = 1.56$ M Temperature 25°

[m-xylene]/M	$[\text{m-xylene}]^{\frac{1}{2}}$	10^4 k(obs.)/mol$^{\frac{1}{2}}$ l$^{-\frac{1}{2}}$ s^{-1}
0.014	0.118	0.44
0.037	0.192	0.68
0.080	0.282	1.33
0.186	0.431	1.72
0.339	0.582	1.96
0.542	0.736	2.46
0.659	0.812	2.70
0.774	0.880	2.75

$[I_2]_o = 1.24 \times 10^{-3}$ M $[NaNO_2] = 0.005$ M

$[HNO_3] = 1.26$ M Temperature 25°

[m-xylene]/M	$[\text{x-xylene}]^{\frac{1}{2}}$	10^4 k(obs.)/mol$^{\frac{1}{2}}$ l$^{-\frac{1}{2}}$ s^{-1}
0.039	0.198	0.48
0.095	0.308	0.74
0.202	0.449	1.08
0.293	0.541	1.33
0.389	0.624	1.49
0.450	0.681	1.63
0.558	0.747	1.65

TABLE 4 (continued)

$[I_2]_o = 1.24 \times 10^{-3}$ M $[NaNO_2] = 0.005$ M

$[HNO_3] = 0.94$ M Temperature 25°

[m-xylene]/M	$[\text{m-xylene}]^{\frac{1}{2}}$	10^4 k(obs.)/$mol^{\frac{1}{2}}$ $l^{-\frac{1}{2}}$ s^{-1}
0.039	0.198	0.24
0.100	0.316	0.42
0.178	0.422	0.59
0.291	0.539	0.72
0.371	0.609	0.78
0.521	0.722	0.90
0.682	0.826	0.97

TABLE 5

Variation of rate of iodination with concentration of 2-bromoanisole

$[I_2]_o = 1.21 \times 10^{-3}$ M $[NaNO_2] = 0.005$ M

$[HNO_3] = 1.61$ M Temperature 25°

[2-Bromoanisole]/M	10^4 k(obs.)/$mol^{\frac{1}{2}}$ $l^{-\frac{1}{2}}$ s^{-1}
0.048	0.37
0.082	0.53
0.133	0.64
0.204	0.80
0.303	1.03
0.389	1.17

Figure 3. Effect of m-xylene concentration on the rate of iodination.

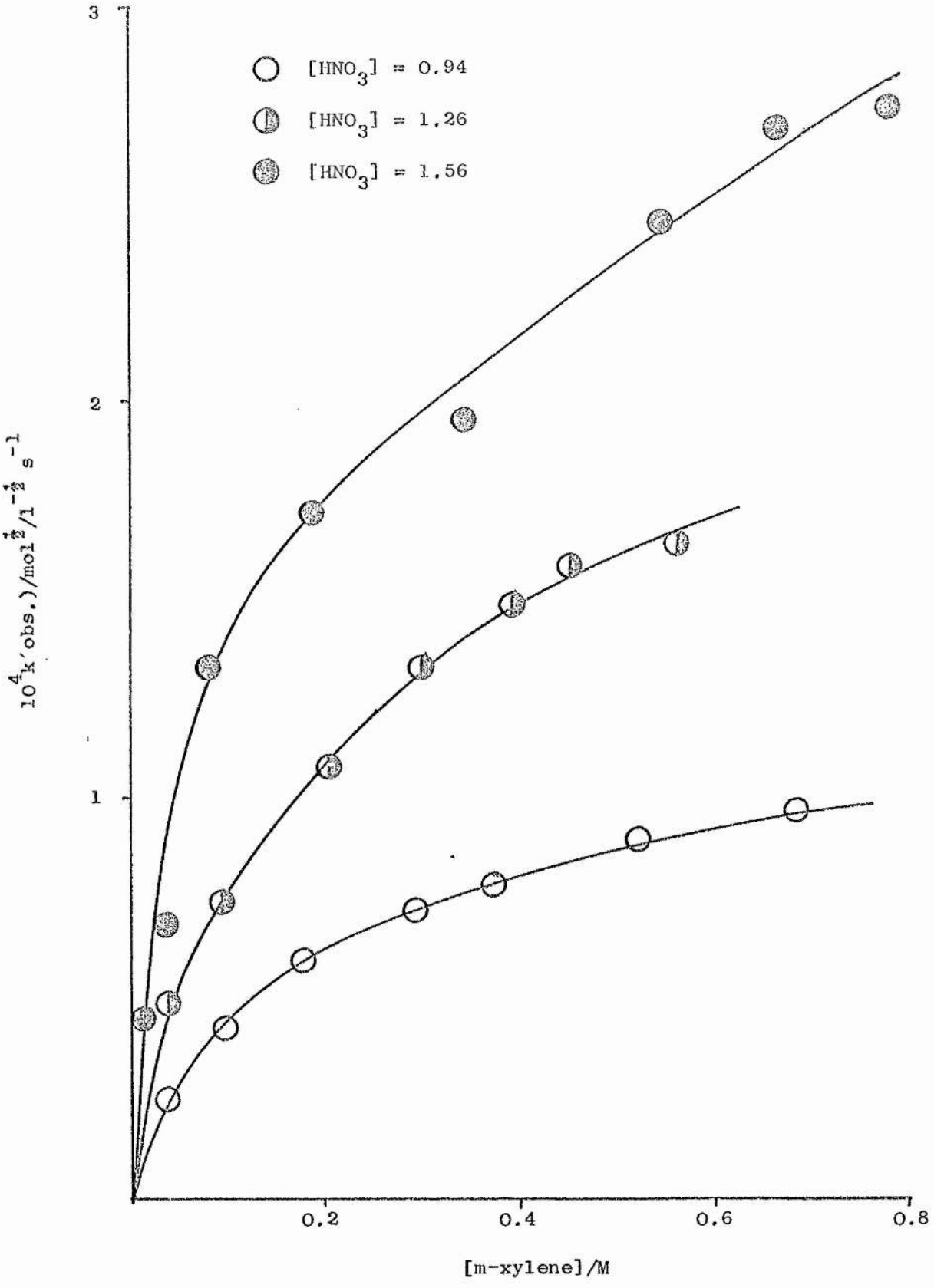


Figure 4. Effect of 2-bromoanisole concentration on rate of iodination.

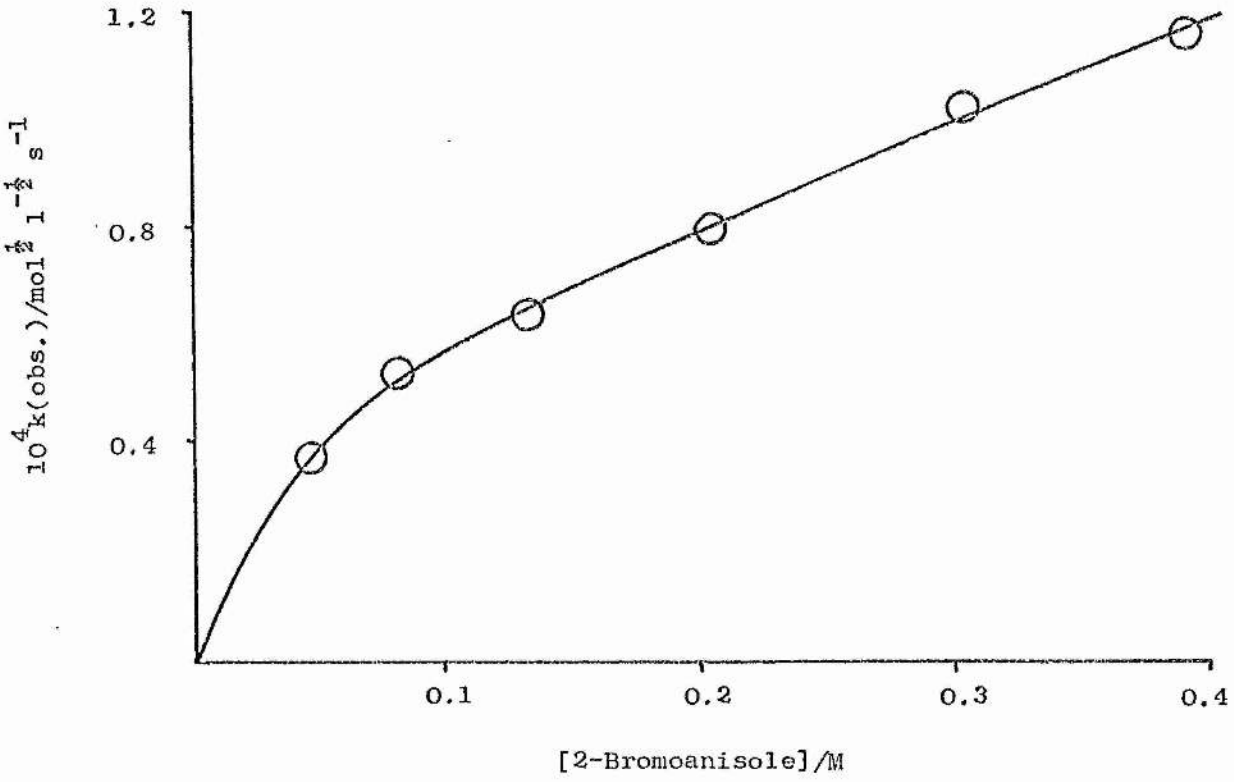


TABLE 6

Variation of rate of iodination with concentration of mesitylene

$[I_2]_o = 1.26 \times 10^{-3}$ M
$[HNO_3] = 1.56$ M
$[NaNO_2] = 0.005$ M
Temperature 25°

[Mesitylene]/M	10^4 k(obs.)/mol$^{\frac{1}{2}}$ l$^{-\frac{1}{2}}$ s^{-1}
0.006	2.39
0.009	3.23
0.017	4.07
0.022	4.81
0.027	5.25
0.034	6.19

$[I_2]_o = 1.24 \times 10^{-3}$ M
$[HNO_3] = 0.94$
$[NaNO_2] = 0.005$ M
Temperature 25°

[Mesitylene]/M	10^4 k(obs.)/mol$^{\frac{1}{2}}$ l$^{-\frac{1}{2}}$ s^{-1}
0.012	1.26
0.030	2.20
0.040	2.32
0.043	2.34
0.058	2.61
0.074	2.95
0.094	3.28

Figure 5. Variation of rate of iodination with concentration of mesitylene.

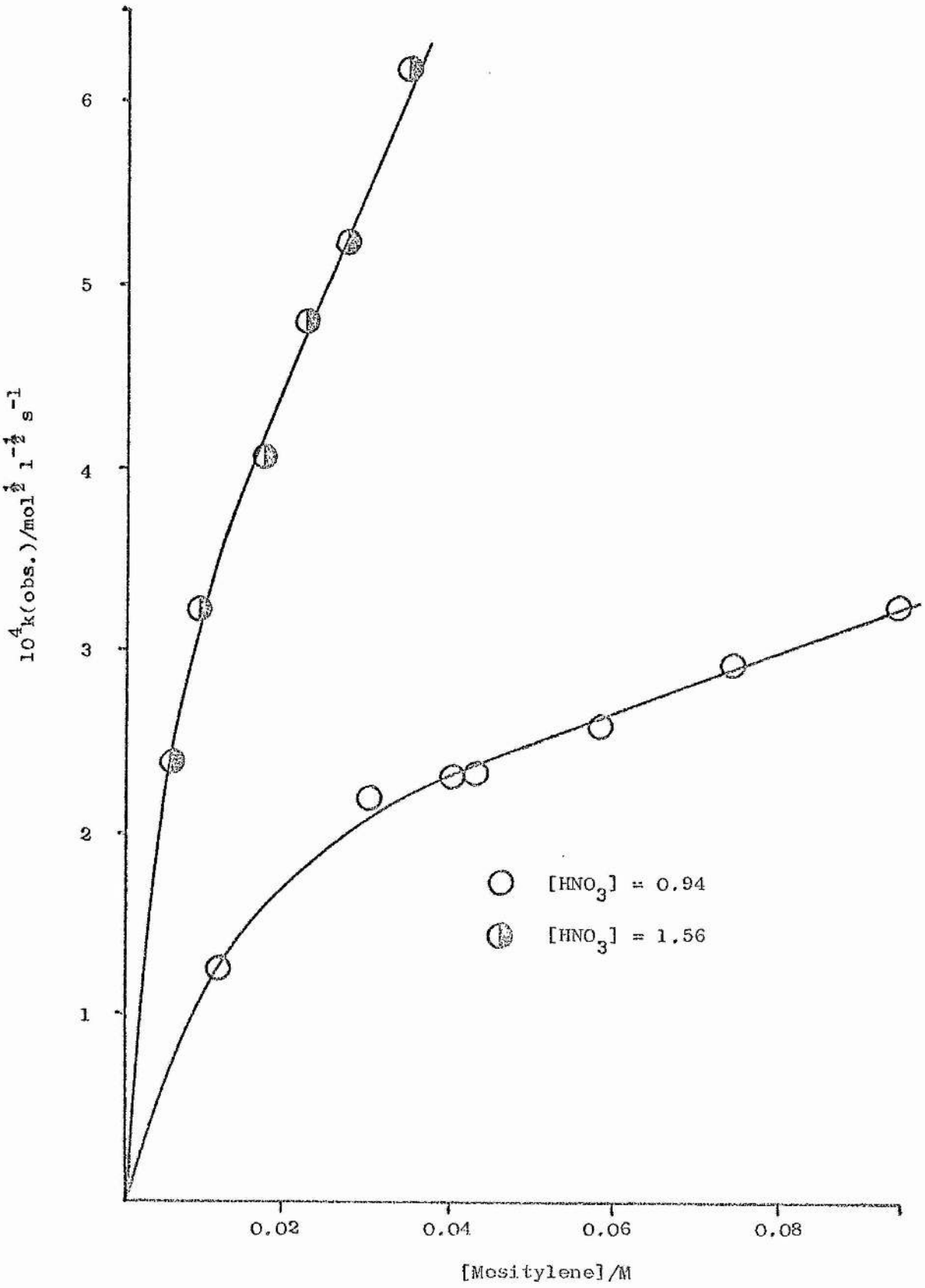


TABLE 7

Variation of rate of iodination with concentration of thiophen

$[I_2]_o = 1.23 \times 10^{-3}$ M $[NaNO_2] = 0.005$ M

$[HNO_3] = 0.16$ M Temperature 25°

[Thiophen]/M	10^4 k(obs.)/mol$^{\frac{1}{2}}$ l$^{-\frac{1}{2}}$ s^{-1}
0.019	0.96
0.064	1.45
0.131	2.10
0.249	2.67
0.379	3.50
0.640	5.14
0.863	6.17

TABLE 8

Variation of rate of iodination with concentration 2-chlorothiophen

$[I_2]_o = 1.24 \times 10^{-3}$ M $[NaNO_2] = 0.005$ M

$[HNO_3] = 0.16$ M Temperature 25°

[2-Chlorothiophen]/M	10^4 k(obs.)/mol$^{\frac{1}{2}}$ l$^{-\frac{1}{2}}$ s^{-1}
0.045	0.42
0.139	0.70
0.319	1.04
0.488	1.28
0.702	1.53

Figure 6. Variation of rate of iodination with concentration of thiophen.

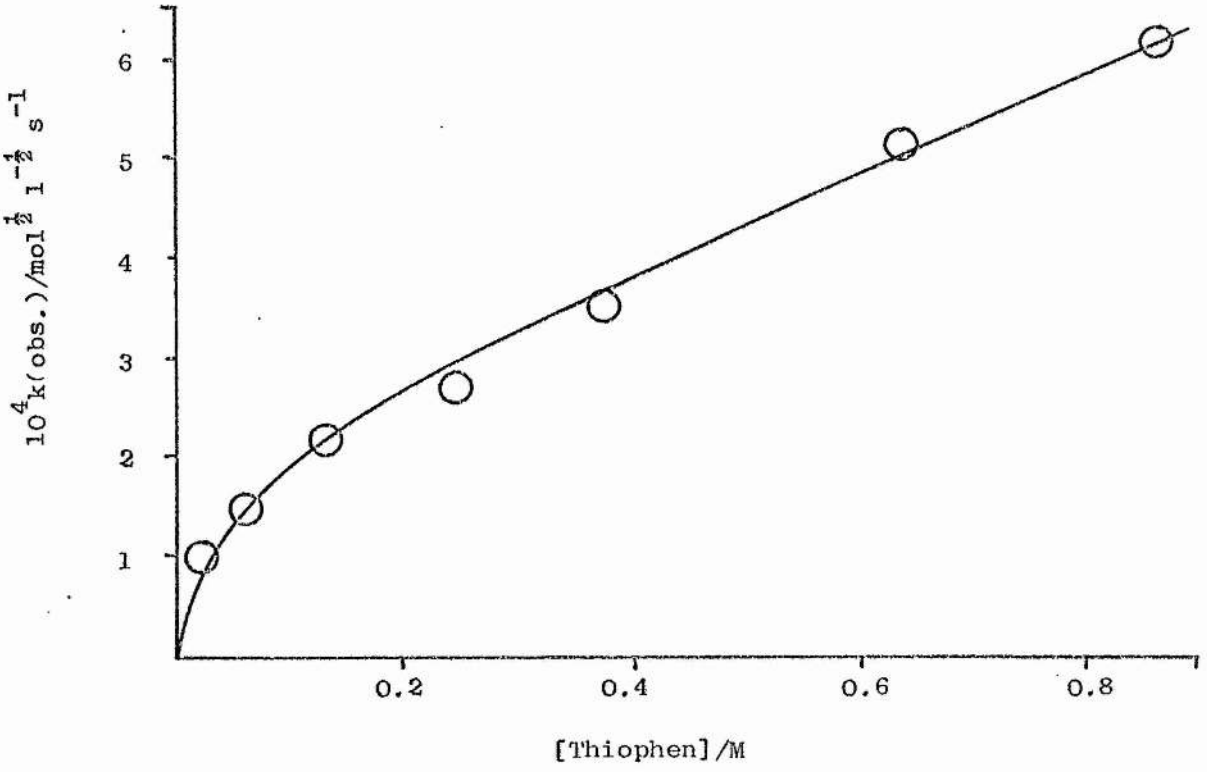


Figure 7. Variation of rate of iodination with concentration of 2-chlorothiophen.

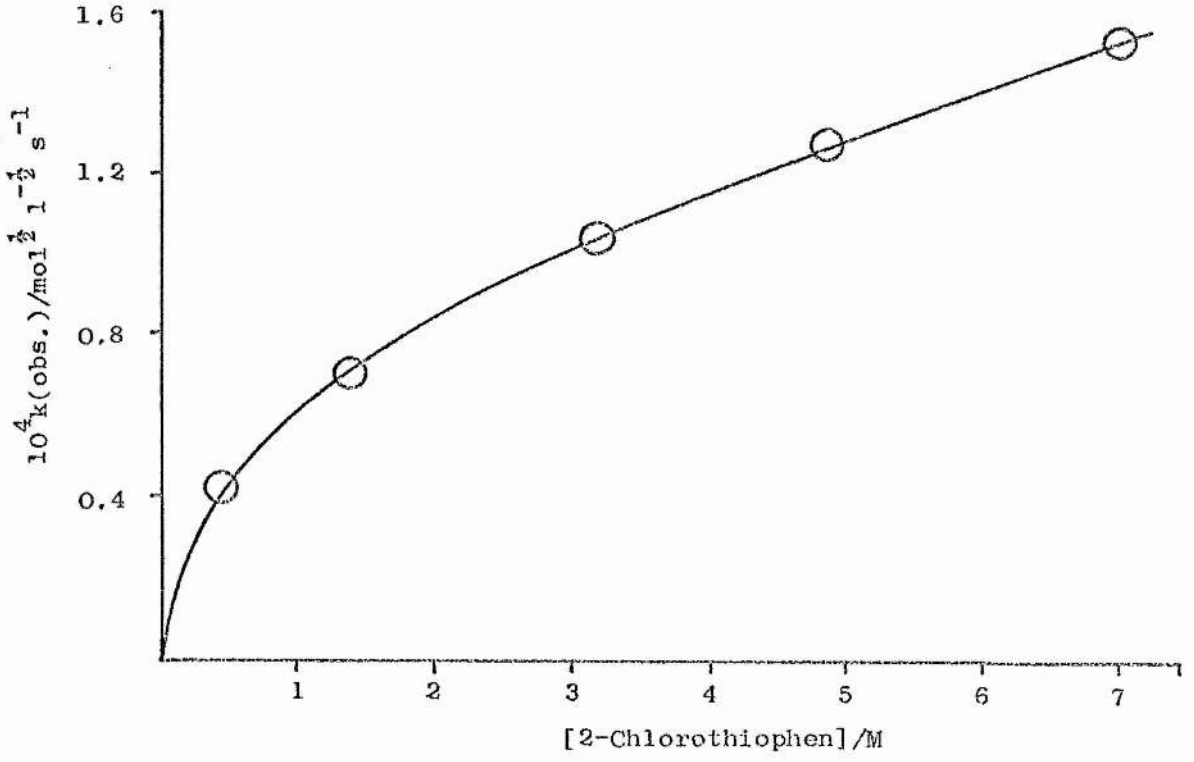
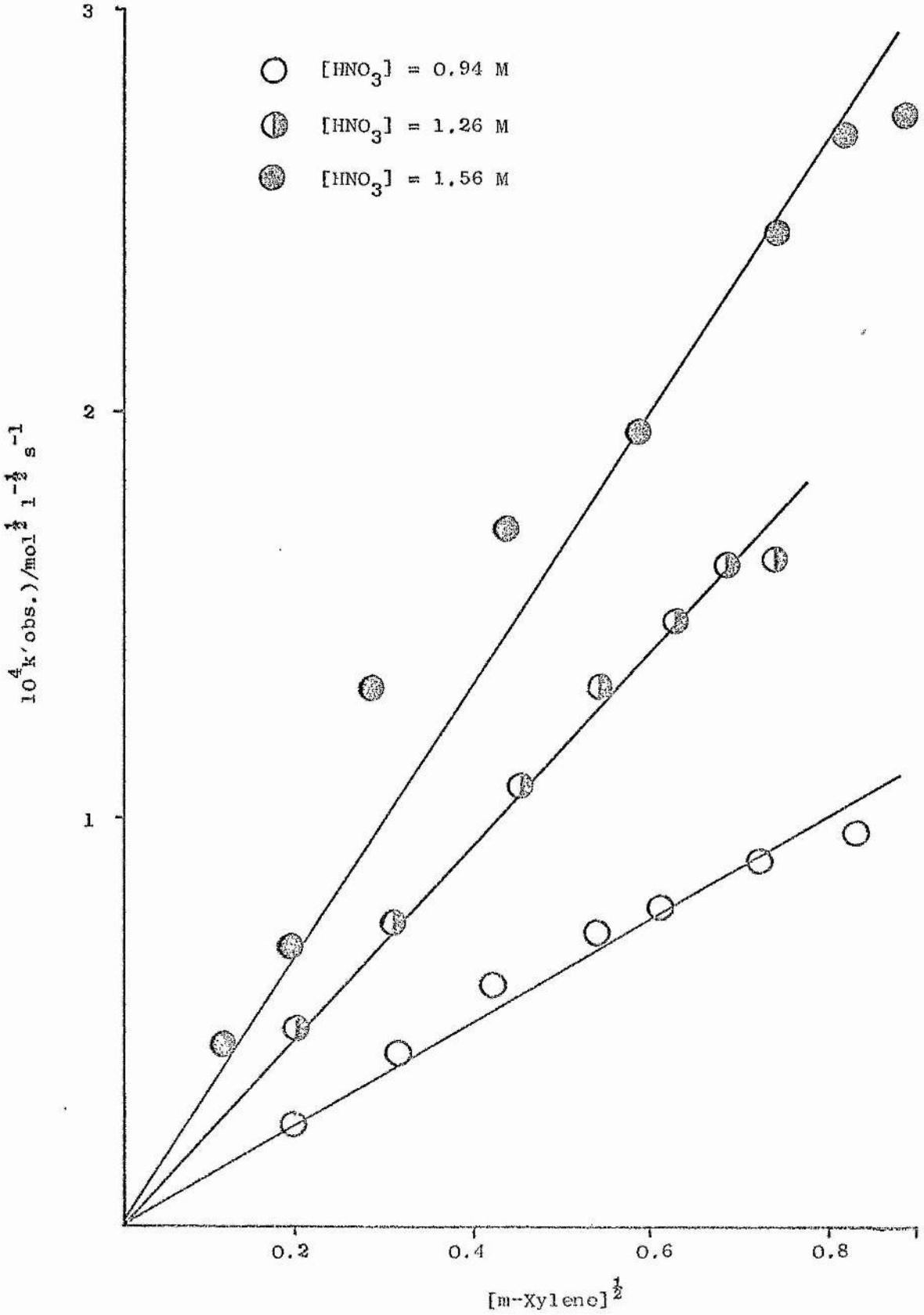


Figure 8. Dependence of k(obs.) on $[m\text{-xylene}]^{\frac{1}{2}}$.



with the substrate and if the iodinating species contains monatomic iodine or NO_2.

Let the iodinating species be designated 'NO_2I'.

Then let the rate determining step be:

$$\text{Substrate} + \text{'}NO_2I\text{'} \xrightarrow{k_1} \text{Substrate.I} + \text{'}NO_2H\text{'}$$

Therefore rate = k_1 [Substrate]['NO_2I']

If the iodinating species is formed by

$$N_2O_4 + I_2 \underset{}{\overset{K_1}{\rightleftharpoons}} 2\text{'}NO_2I\text{'}$$

rate = $k_1K_1^{\frac{1}{2}}$ $[N_2O_4]^{\frac{1}{2}}[I_2]^{\frac{1}{2}}$ [Substrate]

Let us consider the case where iodine forms a charge-transfer complex with the substrate;

$$\text{Substrate} + I_2 \overset{K_2}{\rightleftharpoons} \text{Substrate.}I_2$$

Now substituting in the rate equation for $[I_2]^{\frac{1}{2}}$ will result in the Substrate term becoming [Substrate]$^{\frac{1}{2}}$.

A similar scheme can be worked out for the complexing of dinitrogen tetroxide with substrate.

The precise mathematics of these schemes is somewhat more complicated than this, but it seemed worthwhile to investigate these charge-transfer complexes to find out if their formation could affect the kinetics in this way.

Charge-transfer complexes between iodine and aromatic hydrocarbons are well known[128] and such complexes do exist in acetic acid[129]. However, values of the relevant equilibrium constants were not available from previous studies. Therefore the equilibrium constant, (K), for the formation of such a complex between iodine and m-xylene in glacial acetic acid, was determined by the method of Andrews and Keefer[130]. The value of K was found to be 0.04 l mol^{-1}, this means that under the conditions of the kinetic experiments ([m-xylene] = ca. 0.5 M) the amount of iodine

present as the complex is negligible and the formation of such a complex cannot explain the variation of k(obs.) with the concentration of aromatic compound.

This was confirmed by another series of experiments. Had formation of a charge-transfer complex been the correct explanation, addition of a hydrocarbon which complexes with iodine but does not undergo iodination should lower the rate. Addition of hexamethylbenzene, which readily forms charge-transfer complexes, produced only a small decrease in rate and its effect was about the same as that obtained by addition of hexa-ethylbenzene, which is known to form only a very weak charge-transfer complex with iodine for steric reasons[131].

Complexes between an aromatic hydrocarbon and dinitrogen tetroxide have been reported by Addison[132] but have not been studied as extensively as those with iodine. Addison and Sheldon[126] quote values for the molar extinction coefficients for a number of such complexes and examination of the reaction mixtures used in the kinetic runs, over the appropriate range of wavelengths, indicated that complex formation is negligible and this also must be rejected as an explanation of the dependence of rate on concentration of substrate.

At this stage doubt was cast on the validity of the square-root dependence, in spite of its general and precise applicability. It was decided, therefore, to see if the effect persisted on changing the reaction medium. Nitromethane was rejected since it is immiscable with the sodium nitrite solution, but a 1:1 mixture of acetic acid and trifluoroacetic acid was found to be suitable. In this medium the reaction is much faster[7], and it

TABLE 9

Variation of rate of iodination with concentration of toluene in acetic acid/trifluoroacetic acid

$[I_2]_o$ = 1.08 M
$[HNO_3]$ = 1.61 M
$[NaNO_2]$ = 0.005 M
Temperature 25°

[Toluene]/M	10^4 k(obs.)/$mol^{\frac{1}{2}}$ $l^{-\frac{1}{2}}$ s^{-1}
0.050	1.74
0.103	3.34
0.191	4.20
0.291	4.36
0.432	4.98
0.551	5.32
0.746	6.04

TABLE 10

Variation of rate of iodination with concentration of 2-phenylthiophen

$[I_2]_o$ = 1.23 x 10^{-3} M
$[HNO_3]$ = 0.161 M
$[NaNO_2]$ = 0.005 M
Temperature 25°

[2-Phenylthiophen]/M	10^4 k(obs.)/$mol^{\frac{1}{2}}$ $l^{-\frac{1}{2}}$ s^{-1}
0.0045	5.24
0.0075	8.08
0.0151	10.28
0.0300	11.36
0.0451	10.76
0.0601	11.36
0.0751	10.88
0.113	11.44

Figure 9. Variation of rate of iodination with concentration of toluene.

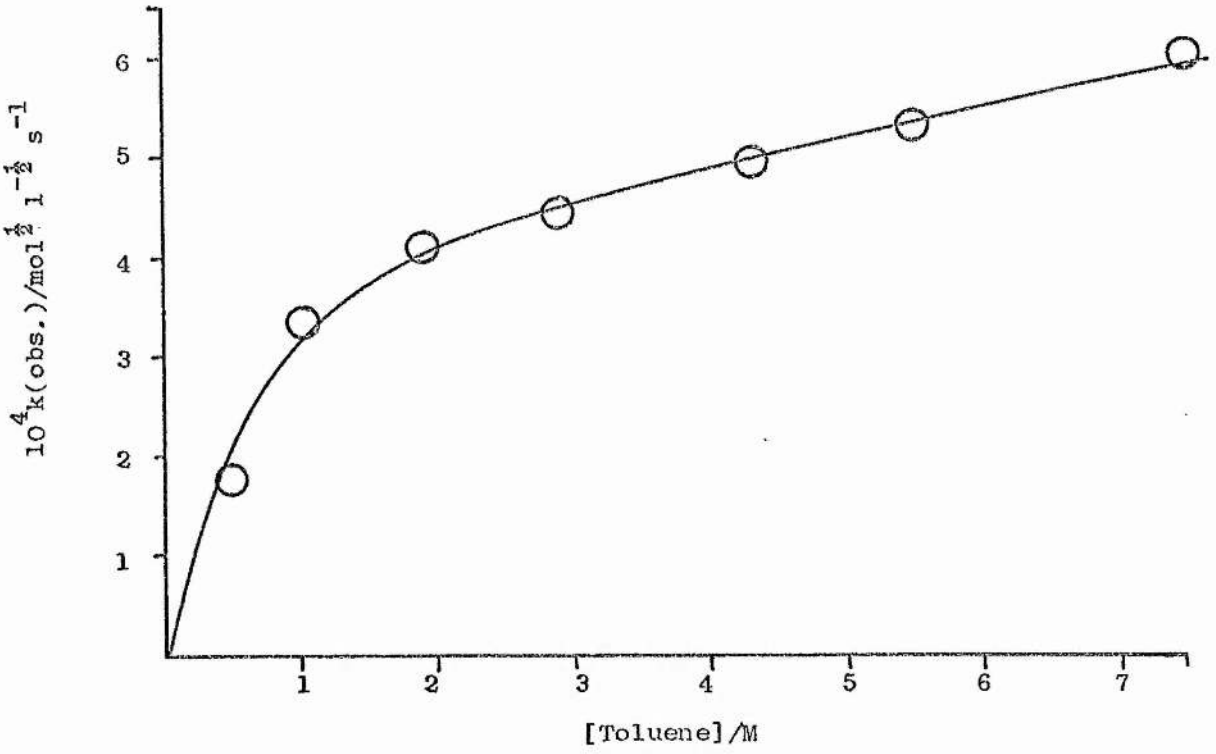


Figure 10. Variation of rate of iodination with concentrations of 2-phenylthiophen.

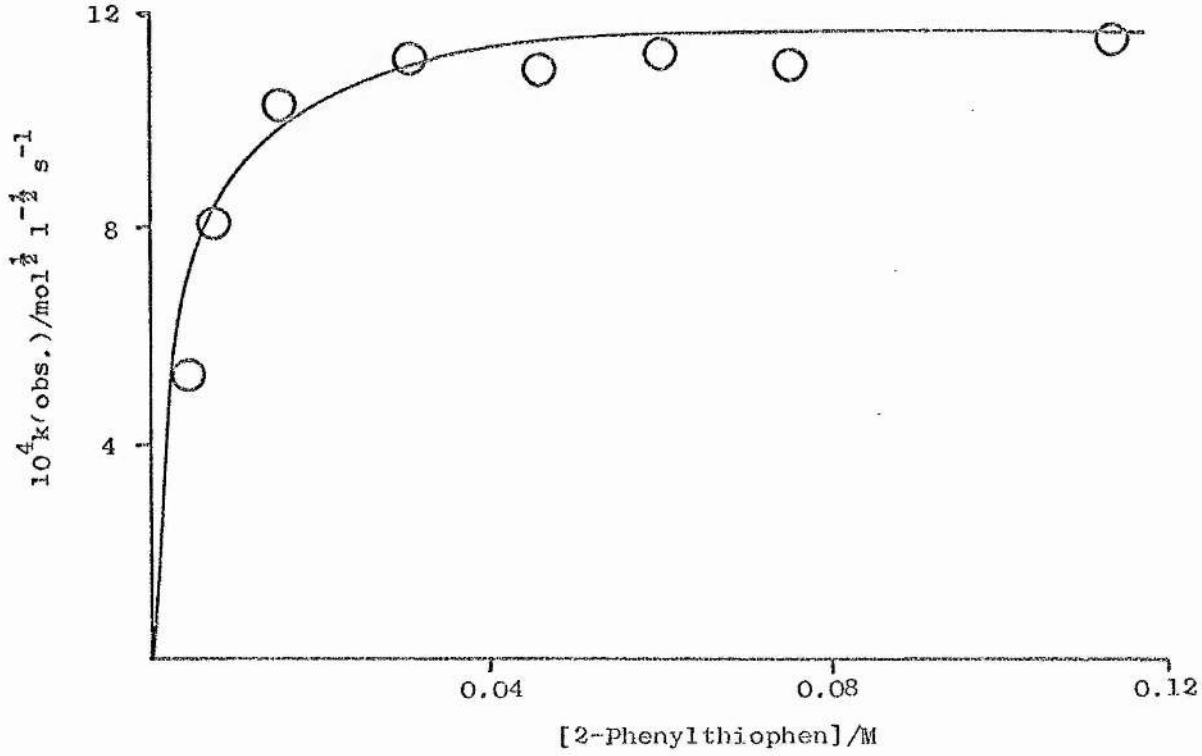


TABLE 11

Effect of m-xylene concentration on the rate of iodination in the presence of dinitrogen tetroxide and perchloric acid

$[I_2]_o = 11.1 \times 10^{-3}$ M
$[HClO_4] = 0.24$ M
$[N_2O_4] = 0.005$ M
Temperature 25°

[m-xylene]/M	10^4 k(obs.)/mol$^{\frac{1}{2}}$ l$^{-\frac{1}{2}}$ s^{-1}
0.041	0.14
0.082	0.28
0.164	0.45
0.390	0.56
0.576	0.67
0.822	0.74

TABLE 12

Effect of added benzene on the rate of iodination of m-xylene.

$[HNO_3] = 1.56$ M
[m-Xylene] = 0.041 M
$[NaNO_2] = 0.005$ M
Temperature 25°

[Benzene]/M	10^5 k(obs.)/mol$^{\frac{1}{2}}$ l$^{-\frac{1}{2}}$ s^{-1}
0.0	7.68
0.33	7.28
0.66	6.76
1.10	6.24

Figure 11. Effect of m-xylene concentrations on the rate of iodination in the presence of dinitrogen tetroxide and perchloric acid.

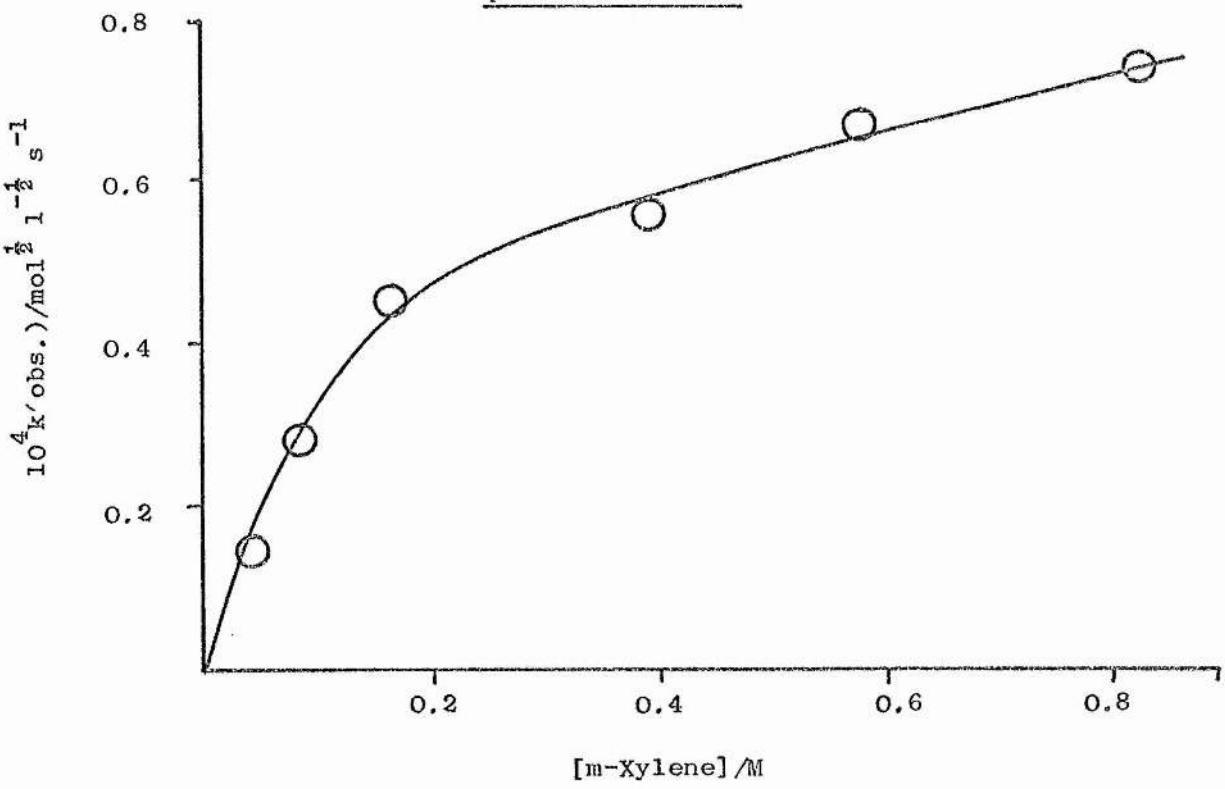
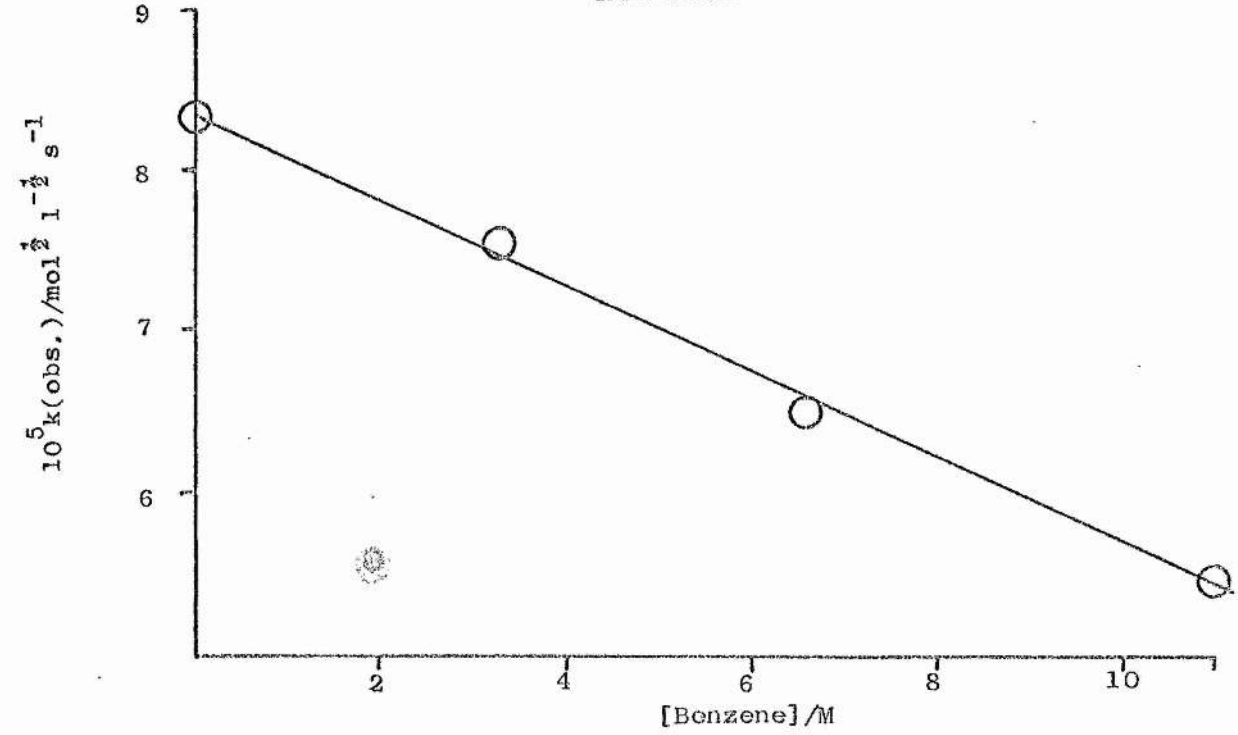


Figure 12. Effect of added benzene on the rate of iodination of m-xylene.



was possible to study the iodination of toluene, a reaction that is too slow to follow in glacial acetic acid. The variation of rate of iodination with concentration of toluene is shown in Figure 9 (see Table 9): the relationship is not linear but neither is that of k(obs.) and the square-root of the toluene concentration. The invalidity of the square-root relationship was further shown by the iodination of the very reactive substrate 2-phenylthiophen and the variation of rate with this substrate is shown in Figure 10 (Table 10). It was concluded, therefore that the square-root relationship observed previously is fortuitous. It is unlikely that the behaviour observed is due to a change of the iodinating species, since the catalysis by acid and sodium nitrite and the half-order kinetics with respect to iodine are found at both high and low concentrations of substrate.

It is possible that the fall-off in the increase of k(obs.) observed at high concentrations of substrate is a medium effect. Therefore, the effect of adding an unreactive aromatic hydrocarbon (benzene) on the rate of iodination of m-xylene was studied. The results are shown in Figure 12 (Table 12) and indicate that, although there is an effect in the right direction, it is too small to provide a satisfactory explanation.

The effect of varying the concentration of m-xylene on the rate of iodination in the presence of dinitrogen tetroxide and perchloric acid, rather than nitric acid and sodium nitrite is shown in Figure 11 (Table 11). The behaviour is essentially the same as that observed previously and from this it was concluded that the species responsible for formation of the iodinating agent are iodine, dinitrogen tetroxide, and an acid.

The rate of iodination of 2-deuterio-5-phenylthiophen was

compared with that of 2-phenyl thiophen (Table 13) at high and low substrate concentration. At low substrate concentration there was an isotope effect of k_H/k_D of 1.35 while at high substrate concentration the value of k_H/k_D was found to be 1.06 indicating essentially no isotope effect.

TABLE 13

Comparison of the rates of iodination of 2-deuterio-5-phenylthiophen and 2-phenylthiophen

$[I_2]_o = 1.24 \times 10^{-3}$ M $[NaNO_2] = 0.005$ M
$[HNO_3] = 0.16$ M Temperature 25°

Substrate	Concentration/M	10^4 k(obs.)/mol$^{\frac{1}{2}}$ l$^{-\frac{1}{2}}$ s^{-1}
2-Phenylthiophen	0.01	8.4
2-Phenylthiophen	0.06	11.04
2-Deuterio-5-phenylthiophen	0.01	6.24
2-Deuterio-5-phenylthiophen	0.06	10.44

There are some miscellaneous observations. The rate of reaction is essentially unaffected by addition of lithium salts and iodoxylene, the latter indicating that there is no catalysis by the products as was found by Ogata and Aoki[8] in their work on the iodination of m-xylene with iodine and peracetic acid. The initial spectrum of the reaction mixture was found to be a superposition of the separate spectra of iodine, substrate, dinitrogen tetroxide, and nitric acid all in acetic acid as solvent indicating that there is no substantial reaction between any of the reactants before iodination. 4-Nitrosotoluene was found not to react with iodine and nitric acid in acetic acid, indicating that nitrosation is not a stop in the iodination process.

The results obtained indicate that the iodinating species is electrophilic and results from protonation of a species formed from iodine and dinitrogen tetroxide and that the rate-determining step involves the aromatic compound. Autocatalysis is due to formation of nitrous acid or dinitrogen tetroxide during the reaction and this must occur in, or after, the step involving the substrate. If reaction between iodine and dinitrogen tetroxide produced the iodinating species and nitrous acid, the latter would react with the excess of nitric acid to give dinitrogen tetroxide and free iodine should disappear, even in the absence of a substrate. This was found not to be the case. On these grounds hypoiodous acid and acetyl hypoiodite, both of which have been postulated by Ogata and Nakajima[7] for iodination in the presence of peracetic acid, were eliminated as possible iodinating species. Another possibility is I^+, but attack by this species on the substrate could not result in formation of nitrous acid, which is necessitated by the autocatalytic nature of the reaction.

The only scheme which accommodates all the experimental observations is that shown by reactions [1]-[4].

$$N_2O_4 \underset{}{\overset{K_1}{\rightleftharpoons}} 2NO_2 \qquad [1]$$

$$NO_2 + H^+ \overset{K_2}{\rightleftharpoons} NO_2H^+ \qquad [2]$$

$$NO_2H^+ + \tfrac{1}{2}I_2 \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} HNO_2I^+ \qquad [3]$$

$$ArH + HNO_2I^+ \xrightarrow{k_4} ArI + HNO_2 + H^+ \qquad [4]$$

Where ArH represents a substituted benzene or thiophen compound.

The variation of k(obs.) with concentration of the substrate can be explained if it is assumed that k_{-3} and k_4 are of comparable magnitude while other equilibria [1] and [2] are established rapidly. Applying the steady state approximation equations [5] - [8]

are obtained.

$$\frac{d[HNO_2I^+]}{dt} = 0$$

$$= k_3[NO_2H^+][I_2]^{\frac{1}{2}} - k_{-3}[HNO_2I^+] - k_4[ArH][HNO_2I^+] \quad [5]$$

$$[HNO_2I^+] = \frac{k_3[NO_2H^+][I_2]^{\frac{1}{2}}}{k_{-3} + k_4[ArH]} \quad [6]$$

$$\text{Rate} = k_4[ArH][HNO_2I^+] \quad [7]$$

$$= \frac{k_4k_3[NO_2H^+][I_2]^{\frac{1}{2}}[ArH]}{k_{-3} + k_4[ArH]} \quad [8]$$

Substituting for $[NO_2H^+]$ from equations [1] and [2] equations [9] and [11] are obtained.

$$\text{Rate} = k_4k_3K_2K_1^{\frac{1}{2}}[H^+][N_2O_4]^{\frac{1}{2}}[I_2]^{\frac{1}{2}}[ArH] \quad [9]$$

$$= k(\text{obs.})\,[I_2]^{\frac{1}{2}} \quad [10]$$

$$k(\text{obs.}) = \frac{k_4k_3K_2K_1^{\frac{1}{2}}[H^+][N_2O_4]^{\frac{1}{2}}[ArH]}{k_{-3} + k_4[ArH]} \quad [11]$$

Equation [11] shows that k(obs.) should be a linear function of $[H^+]$, which in concentrated acid is best represented by the acidity function h_o, and also to have a fairly complex dependence upon [ArH].

Transformation of equation [11] gives equation [12];

$$k(\text{obs.}) = k_2K_2K_1^{\frac{1}{2}}[N_2O_4]^{\frac{1}{2}}[H^+] - \frac{k(\text{obs.})\,k_{-3}}{k_4\,[ArH]} \quad [12]$$

so that a plot of k(obs.) against k(obs.)/[ArH] should be linear with a slope of $-k_{-3}/k_4$ and an intercept of $k_3K_2K_1^{\frac{1}{2}}[N_2O_4]^{\frac{1}{2}}[H^+]$. This linearity was found with all substrates studied at varying acidities and two typical examples for, xylene, see Figure 13 (Table 14) and toluene, see Figure 14 (Table 15), are given. The case of 2-phenylthiophen is notable in that the value of k(obs.)

TABLE 14

Values of k(obs.) and k(obs.)/[ArH] for the iodination of m-xylene

$[NaNO_2]$ = 0.005 M	$[HNO_3]$ = 0.94 M
$10^4 k(obs.)/mol^{\frac{1}{2}}\ l^{-\frac{1}{2}}\ s^{-1}$	$10^4 k(obs.)/[m\text{-xylene}]/mol^{-\frac{1}{2}}\ l^{\frac{1}{2}}\ s^{-1}$
0.24	6.12
0.42	4.09
0.59	3.32
0.72	2.48
0.78	2.10
0.97	1.42

TABLE 15

Values of k(obs.) and k(obs.)/[ArH] for the iodination of toluene

$[NaNO_2]$ = 0.005 M $[HNO_3]$ = 1.61 M

Solvent: 1:1 mixture of acetic acid and trifluoroacetic acid

$10^4 k(obs.)/mol^{\frac{1}{2}}\ l^{-\frac{1}{2}}\ s^{-1}$	$10^4 k(obs.)/[Toluene]/mol^{-\frac{1}{2}}\ l^{\frac{1}{2}}\ s^{-1}$
1.74	34.9
3.37	22.0
4.36	15.0
4.98	11.5
5.32	9.7
6.04	8.1

Figure 13. Plot of k(obs.) against k(obs.)/[m-Xylene].

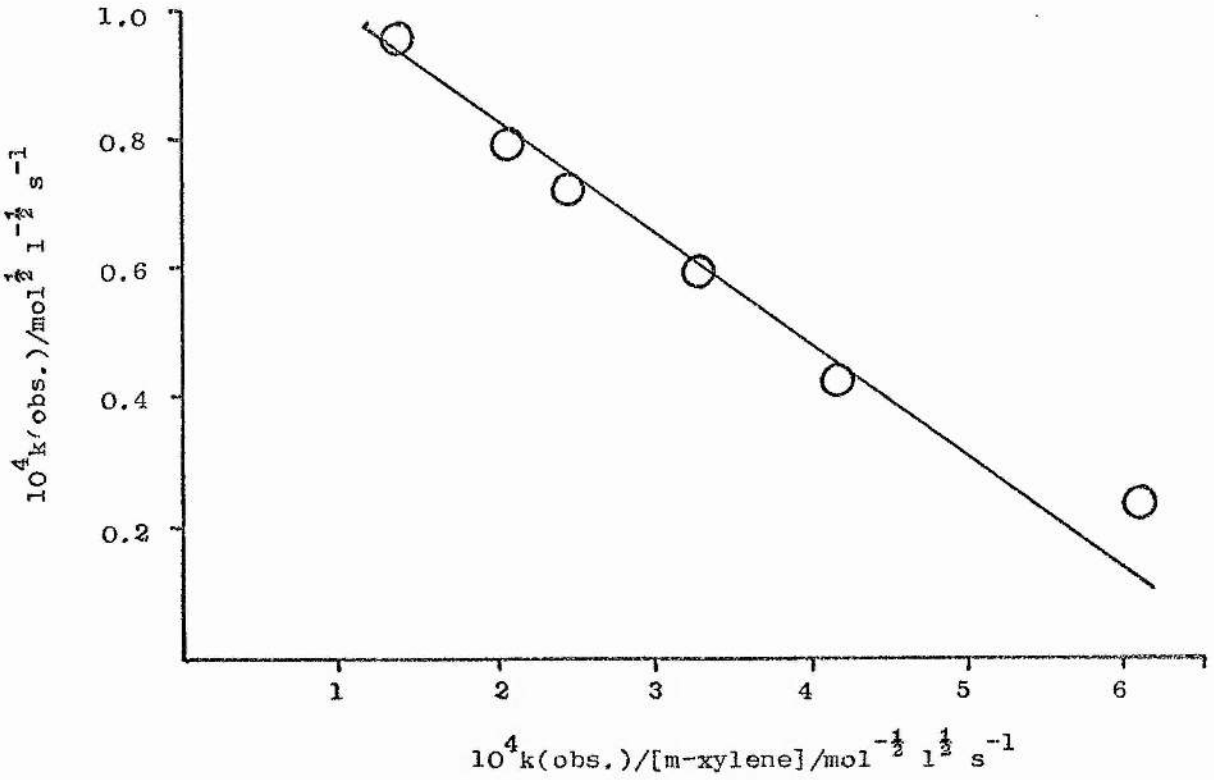
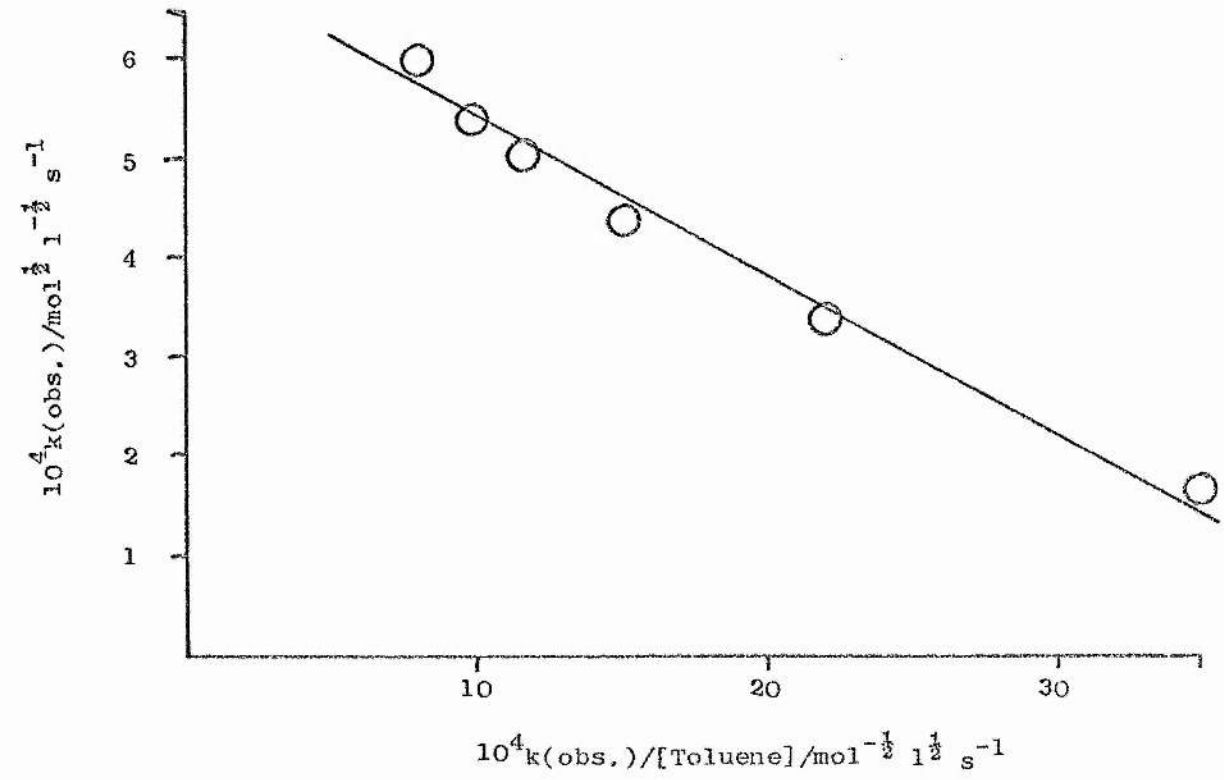


Figure 14. Plot of k'obs.) against k(obs.)/[Toluene].



becomes almost independent of substrate at higher concentrations. This is to be expected by consideration of equation [11], if the term $k_4[ArH]$ becomes considerably larger than k_{-3} the equation tends to equation [13];

$$k(obs.) = k_3K_2K^{\frac{1}{2}}[N_2O_4]^{\frac{1}{2}}[H^+] \qquad [13]$$

and the reaction becomes zero-order in substrate. Comparison of the iodination of 2-phenylthiophen and 2-deuterio-5-phenylthiophen shows that at high concentration there is essentially no isotope effect while there is a primary isotope effect at lower concentration, which is consistent with the reaction at high concentration being zero-order in substrate. The primary isotope effect at low concentration indicates that in the iodination reaction in general the rate determining step is the cleavage of a carbon-hydrogen bond, and is consistent with a two step mechanism of the type

$$ArH + E^+ \underset{k_{-a}}{\overset{k_a}{\rightleftharpoons}} {}^+Ar\begin{matrix}H\\E\end{matrix} \xrightarrow{k_b} ArE + H^+$$

where the rate determining step is k_b.

In view of the complexity of the rate equation no deductions concerning the values of the individual rate constants can be made, but the results are entirely consistent with protonated NO_2I as the identity of the iodinating species. Nitryl iodide (NO_2I) has been postulated by Hassner, Kropp, and Kent[47] in the formation of nitroiodides from olefins, iodine and dinitrogen tetroxide. This is a free-radical reaction but the protonated form appears to be the electrophile responsible for aromatic iodination.

Throughout this discussion no differentiation has been made between substituted benzenes and thiophens, this is because all

the effects reported were found in both cases and the one mechanism seems to apply to both substrate types. Similar conclusions were drawn by Butler and Hendry[133,134] in their work on the bromination and chlorination of substituted thiophens.

As a footnote to this work, it is interesting that if iodination using nitric acid were attempted with absolutely pure reactants the yield would be extremely low, and it is only by virtue of the impurities normally present in nitric acid that this method has become a viable synthesis.

2. MECHANISM OF IODINE MIGRATION DURING THE NITRODEIODINATION OF 4-IODOANISOLE

Early work by Reverdin[1] showed that, although nitration of 2-iodoanisole proceeds normally with nitration at the 4-position, nitration of 4-iodoanisole results in formation of 2-iodo-4-nitroanisole in high yield, and thus there is an unexpected migration of the iodine from the 4- to the 2-position. Later, more detailed work by Robinson[2] showed that 2,4-di-iodoanisole is an intermediate in this reaction, and it was proposed that almost all the 2-iodo-4-nitroanisole produced is formed by the initial formation of 2-4-di-iodoanisole and its subsequent nitrodeiodination. This original work involved the use of fuming nitric acid and high concentrations of 4-iodoanisole, conditions unsuitable for a kinetic investigation. Much lower concentrations of substrate (ca. 5×10^{-3} M) and a mixture of equal parts (v/v) of nitric and acetic acids containing sodium nitrite (ca. 0.025 M) were used. The significance of the added nitrite will be discussed later. The product under these conditions was found to be the same as that in the original work, 2-iodo-4-nitroanisole, and was formed in high yield.

Because of the low concentration of substrate, the intermediates occurring during the reaction were identified by an isotopic dilution technique. Analysis of the products of the reaction using [^{14}C]-4-iodoanisole, after 35 s showed that all the starting material had been converted into an approximately equimolar mixture of 2,4-di-iodoanisole and 4-nitroanisole. Clearly rapid nitrodeiodination of 4-iodoanisole had occurred and the iodine thus released (probably not as free iodine but as some electrophilic iodinating species) had iodinated the most reactive substrate present, that is, the unchanged 4-iodoanisole. This part of the reaction is accompanied by the formation of a transient yellow which will be discussed later.

The above experiment was repeated with the reaction mixture having been allowed to stand for 30 min and analysis of the products showed that the 4-iodoanisole had now been converted into an equimolar mixture of 4-nitroanisole and 2-iodo-4-nitroanisole. Thus, in the second stage of the reaction, the 4-nitroanisole remains unchanged but there is complete nitrodeiodination of 2,4-di-iodoanisole at the 4-position. This stage of the reaction is accompanied by the slow formation of molecular iodine.

At this stage the reaction mixture contained iodine and nitric acid, a mixture known to effect aromatic iodination[18]. The most susceptible substrate present was 4-nitroanisole, but this is much deactivated towards electrophilic attack. However, from 30 min onwards there was slow disappearance of the iodine and it seemed probable that this resulted from iodination of 4-nitroanisole at the 2-position to give a product identical with that obtained from the nitrodeiodination of 2,4-di-iodoanisole. This third stage in the reaction was confirmed by nitrating

4-iodoanisole in the presence of [^{14}C]-4-nitroanisole. After 30 min the 2-iodo-4-nitroanisole isolated from the mixture was found to be essentially inactive but after three days, when all the free iodine had disappeared, the activity of the product was consistent with its partial formation via iodination of 4-nitroanisole.

From spectral studies, the maximum concentration of iodine equalled approximately half the initial concentration of 4-iodoanisole, the remaining iodine being present a 2-iodo-4-nitroanisole. The appearance of iodine was found to be of the first order in iodine [k(obs.) = 4.14×10^{-3} s^{-1} at 25°]. Under identical conditions the formation of iodine from 2,4-di-iodoanisole occurred at the same rate [k(obs.) = 4.19×10^{-3} s^{-1}], thus confirming its intermediacy in the reaction. This also indicates that the spectral studies on 4-iodoanisole were in fact observations of the reaction of 2-4-di-iodoanisole and this substrate was used in further spectral studies to avoid unnecessary complications.

The sequence of events occurring in the formation of 2-iodo-4-nitroanisole from 4-iodoanisole has now been established, but the species responsible for deiodination has not been defined. In the presence of urea, which destroys nitrous acid, there is no reaction, while sodium nitrite acts as a catalyst, so that the species responsible for deiodination is probably a nitrosating agent and there is subsequent oxidation of the resulting nitroso-compound to the corresponding nitro-compound. The effect of added sodium nitrite on the rate of formation of iodine from 2,4-di-iodoanisole and nitric acid is shown in Figure 15 (Table 16) and from 4-iodo-2,6-dimethylanisole, an activated substrate where the iodine cannot re-enter the aromatic ring at the 2-position, and nitric acid

is shown in Figure 16 (Table 17). In both of these cases all the iodine originally present in the 4-position of the substrate appears as free iodine at the end of the reaction.

The reaction is also catalysed by acid, and the effect of increased concentration of nitric acid on the rate of deiodination of 4-iodo-2,6-dimethylanisole is shown in Figure 17 (Table 18). The increase in k(obs.) with acid concentration is very sharp and the rate is probably proportional to the acidity function h_o rather than the concentration of acid. This is indicative of attack by a nitrosating species the concentration of which is proportional to the acidity. The conclusion that attack is by a nitrosating species is further substantiated by the fact that nitrosyl hexafluorophosphate, a source of NO^+, readily deiodinates 4-iodoanisole in anhydrous acetic acid, while nitronium tetrafluoroborate, a source of NO_2^+, has very little effect.

The reaction cannot proceed by protodeiodination followed by nitration since 4-iodoanisole remains virtually unreacted even in concentrated perchloric acid. Also protodeiodination of 4-iodoanisole would yield anisole which would be the most reactive substrate present and would therefore be preferentially iodinated or nitrosated. The former process would be equivalent to no overall reaction having occurred and the latter would lead to the intense colours normally associated with the nitrosation of anisole and these are not observed. Finally the proved intermediacy of 2,4-iodoanisole and nitroanisole and their subsequent reactions are consistent with nitroso- or nitrodeiodination but cannot be easily accommodated in a mechanism involving protodeiodination.

TABLE 16

Effect of varying sodium nitrite concentration on the rate of nitrodeiodination of 2,4-di-iodoanisole

$[2,4\text{-Di-iodoanisole}]_o = 2.1 \times 10^{-3}$ M $[HNO_3] = 8.05$ M

Temperature 25°

$[NaNO_2]$/M	$10^3 k(obs.)/s^{-1}$
0.010	1.0
0.020	1.6
0.040	2.4
0.060	3.8
0.080	4.4
0.100	6.3
0.145	9.9

TABLE 17

Effect of varying sodium nitrite concentration on the rate of nitrodeiodination of 4-iodo-2,6-dimethylanisole

$[4\text{-Iodo-2,6-dimethylanisole}]_o = 2.4 \times 10^{-3}$ M $[HNO_3] = 5.64$ M

Temperature 25°

$[NaNO_2]$/M	$10^3 k(obs.)/s^{-1}$
0.003	2.85
0.009	4.15
0.012	6.89
0.022	8.67
0.030	10.4
0.039	14.7

Figure 15. Effect of nitrite concentration on the rate of deiodination of 2,4-di-iodoanisole.

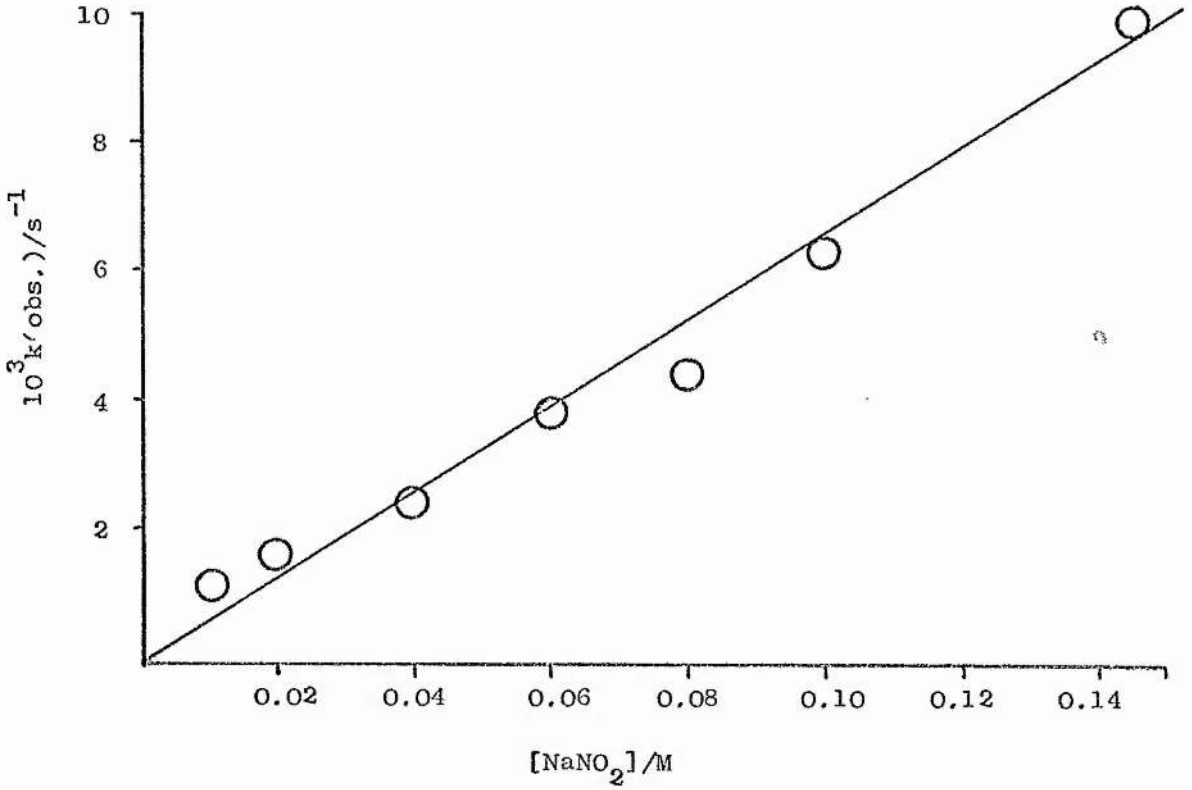


Figure 16. Effect of nitrite concentration on the rate of deiodination of 4-iodo-2,6-dimethylanisole.

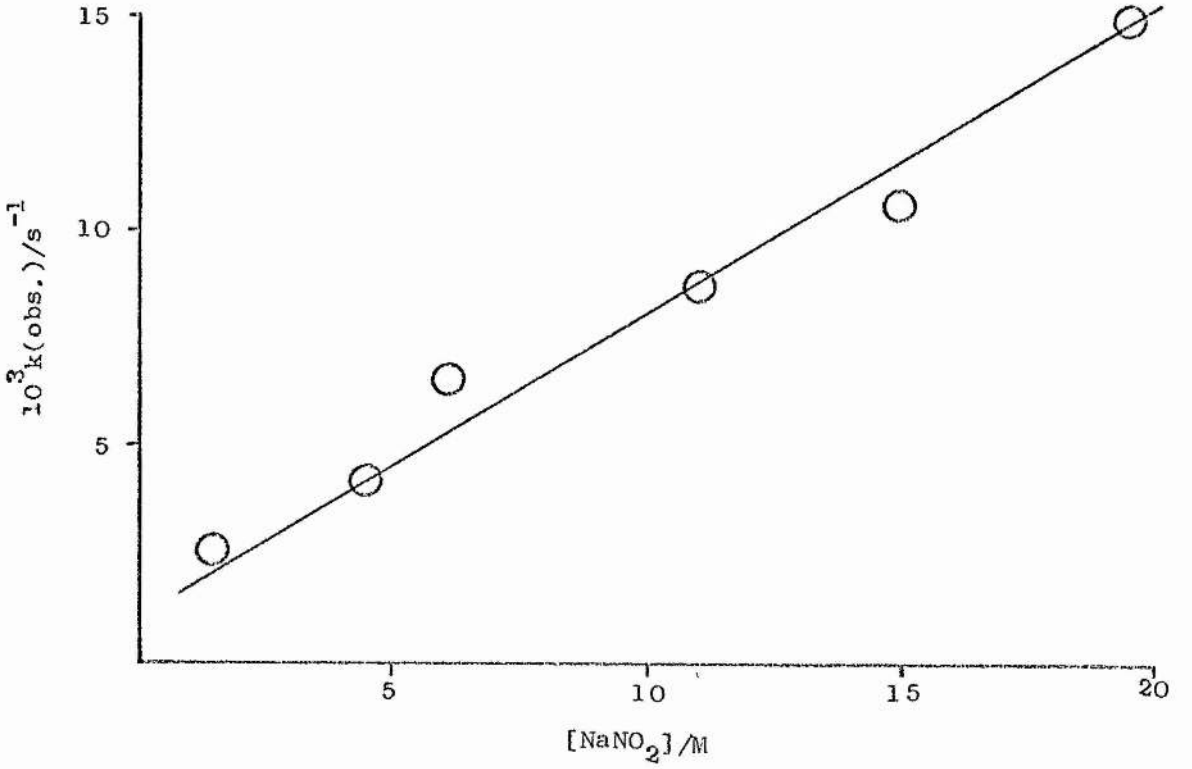


TABLE 18

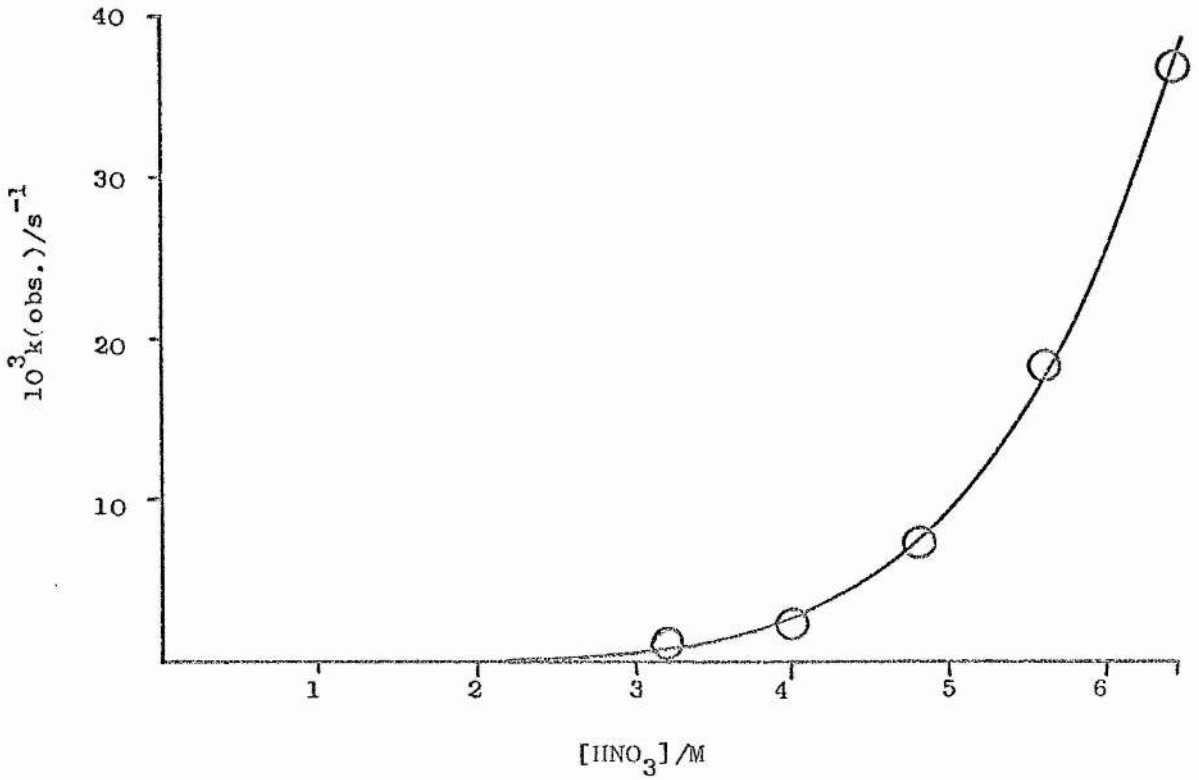
Effect of varying nitric acid concentration on the rate of nitrodeiodination of 4-iodo-2,6-dimethylanisole

$[\text{4-Iodo-2,6-dimethylanisole}]_o = 2.4 \times 10^{-3}$ M $[NaNO_2] = 0.041$ M

Temperature 25°

$[HNO_3]$/M	$10^3 k(\text{obs.})/s^{-1}$
3.22	0.803
4.03	2.09
4.83	7.05
5.64	18.1
6.44	36.5

Figure 17. Effect of nitric acid concentration on the rate of deiodination of 4-iodo-2,6-dimethylanisole.

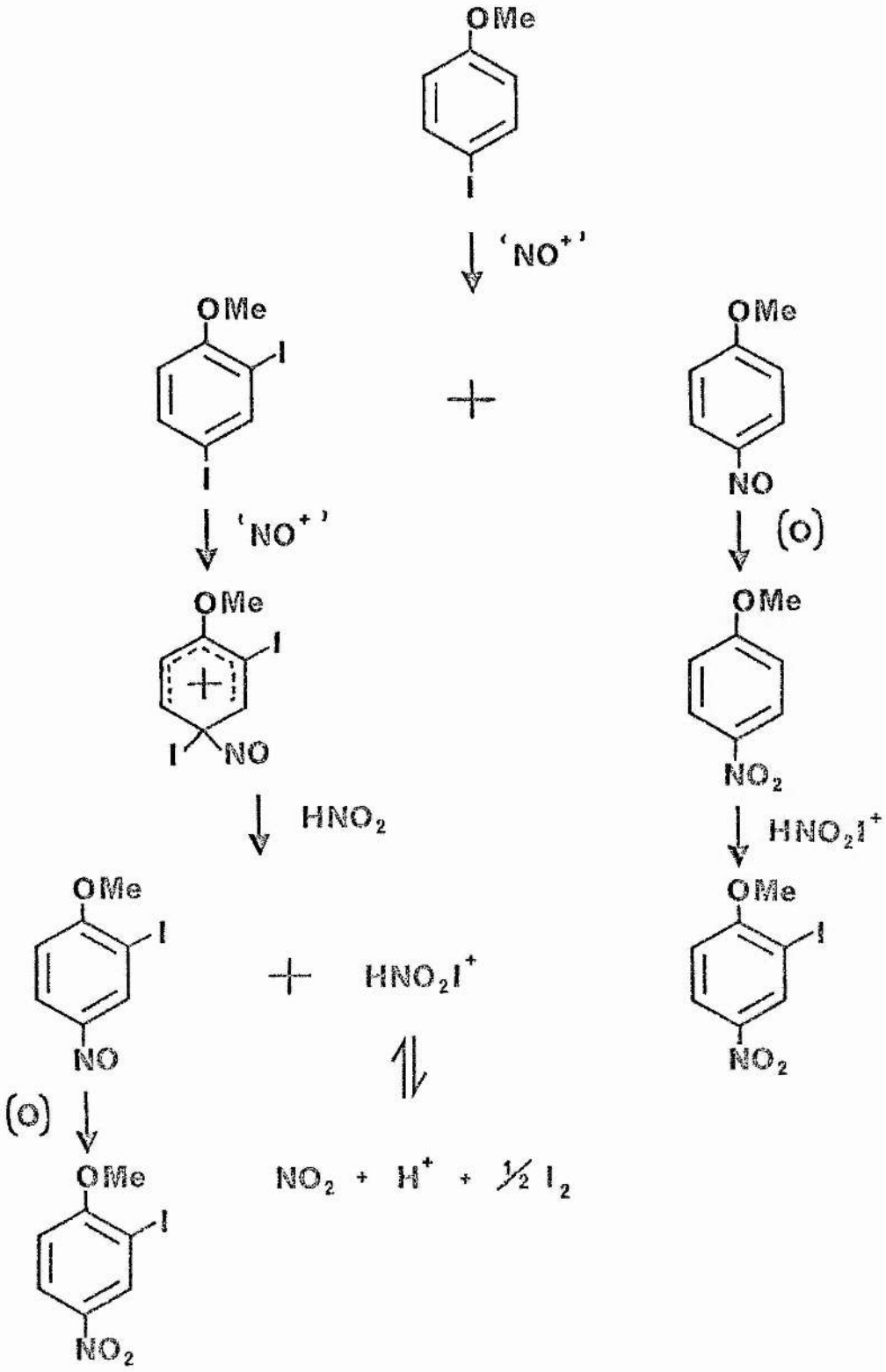


The evidence is, then, that the reaction occurs by attack of a nitrosating species which will be referred to as 'NO^+', although the exact nature of this species is not known. It seems improbable that I^+ will be expelled from the Wheland intermediate in a unimolecular process, but will be removed by some nucleophile present in the reaction mixture and, as is shown by the rapid iodination of 4-iodoanisole in the first stage of the reaction, the resulting species must be able to act as an iodinating agent. With these conditions in mind it is suggested that nitrous acid is the nucleophile which removes I^+ to give HNO_2I^+, which has been postulated as the species responsible for aromatic iodination by iodine and nitric acid previously in this thesis. The suggested mechanism for the complete reaction is shown in the Scheme.

It was hoped that by adding other nucleophiles to the system that one of them might remove I^+ preferentially to nitrous acid and thus, if the removal of I^+ from the Wheland intermediate were the rate determining step, a change in the rate of appearance of molecular iodine would be observed. Various lithium salts were added, since they are soluble in acetic acid, and the anions could then act as the required nucleophile. Essentially no change in k(obs.) was noted, but this result does not indicate whether attack of the nitrosating species or removal of I^+ is the rate determining step since it may have been that none of thenucleophiles added acted in preference to nitrous acid.

One of the puzzling features of the reaction is the selectivity of the 2- and 4-positions of anisole towards nitrodeiodination. It has been assumed throughout that no

Scheme


OMe
I
'NO+'
OMe
I
I
'NO+'
OMe
I
I
NO
HNO2
OMe
I
NO
(O)
OMe
I
NO2
(O)
OMe
I
NO2
OMe
NO
HNO2I+
HNO2I+
NO2 + H+ + ½ I2

reaction occurs at the 2-position because 2-iodoanisole nitrates to give the expected product with no evidence of deiodination. Also, 4-iodo-2-nitroanisole is readily nitrodeiodinated by concentrated nitric acid containing sodium nitrite to give 2,4-dinitroanisole, identified by comparison with an authentic sample, and the release of free iodine is found to be first order when monitored spectrophotometrically, see Figure 18 (Table 19)., while 2-iodo-4-nitroanisole is quite stable in that medium. The very low ortho: para ratio has been confirmed directly by studying the nitration of [^{14}C]-2,4-di-iodoanisole under the same conditions as in the nitration of 4-iodoanisole. Dilution of the product with the two possible isomers indicated that there is 92% attack at the 4-position and only 8% at the 2-position. This parallels exactly the isomer ratio observed by Hoggett et al.[135] for nitration via nitrosation of anisole in 65% sulphuric acid, and is consistent with the view that the initial reaction is nitrosation. It can be seen that since the nitrosating species is a weak electrophile[136] attack will occur more readily at the 4-position since it is more activated than the 2-position, contrasting with a stronger electrophile, such as NO_2^+, which is less discriminating as to its position of attack. However, why such a weak electrophile should displace iodine so readily is not clear but an identical situation has been reported by Eaborn et al[101], who found that little or no nitrodesilylation occurred when p-tolyltrimethylsilane was treated with nitric acid in acetic anhydride in the absence of lower nitrogen oxides, but when such oxides were present nitrodesilylation products were readily formed, apparently via nitrosodesilylation.

Although the nitration of 2- and 4-iodoanisole has been

TABLE 19

Nitrodeiodination of 4-iodo-2-nitroanisole

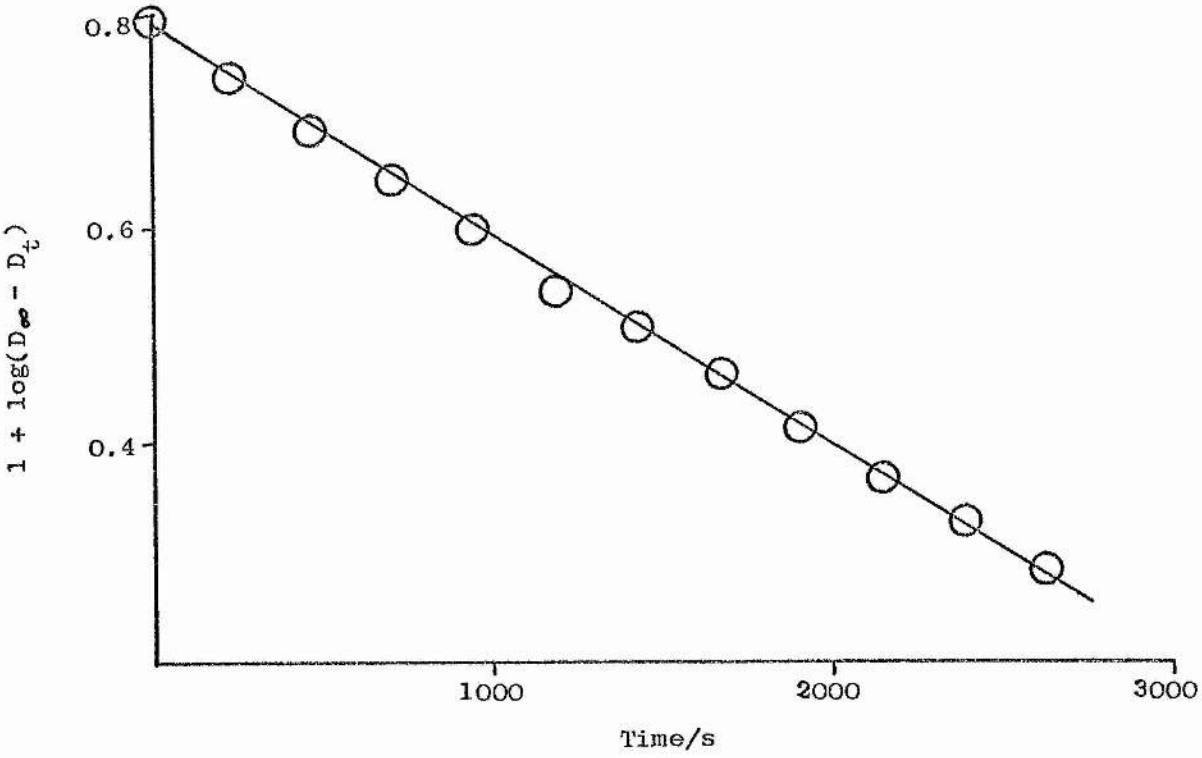
$[4\text{-iodo-2-nitroanisole}]_o = 2.90 \times 10^{-3}$ M $[NaNO_2] = 0.005$ M

$[HNO_3] = 14.2$ M Temperature 25°

Time/s	$(D - D_t)$	$1 + \log(D_\infty - D_t)$
0.0	0.614	0.788
240.0	0.549	0.740
480.0	0.490	0.690
720.0	0.442	0.645
960.0	0.396	0.598
1200.0	0.356	0.539
1440.0	0.322	0.508
1680.0	0.289	0.461
1920.0	0.259	0.413
2160.0	0.232	0.366
2400.0	0.211	0.324
2640.0	0.190	0.279

$k(obs.) = 4.42 \times 10^{-4}\ s^{-1}$

Figure 18. Nitrodeiodination of 4-iodo-2-nitroanisole.

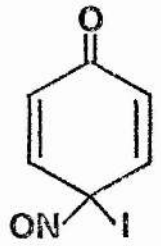


studied[1,2] there is no report of the products of the nitration of 3-iodoanisole. Therefore, to complete this work the nitration of all three isomers under identical conditions was studied. The 2- and 4-isomers both gave rise to 2-iodo-4-nitroanisole as reported and 3-iodoanisole gave rise to a compound which was identified as 3,6-di-iodo-4-nitroanisole a previously unreported compound. When this reaction was not allowed to go to completion but stopped after 60 min, this same product was found, but in lower yield, the main product being 3-iodo-4-nitroanisole, that is the normal nitration product. The di-iodocompound is probably formed by the nitrodeiodination and subsequent iodination of this nitration product, the resulting compound being sufficiently deactivated to withstand further nitrodeiodination. The reaction also gives rise to a number of highly coloured products in low yield which are probably formed by the nitrosation of the intermediates of the main reaction. Thus 3-iodoanisole gives rise to a far more complex series of reactions than do either 2- or 4-iodoanisole which give essentially one product.

It was hoped that nitrodeiodination could be studied in water by using sulphonic acid analogues of anisole. Although deiodination does take place with 2-(4-iodophenoxy)-ethylsulphonic acid the appearance of free iodine tends to be masked by the formation of an intense brown colour which is extremely sensitive to acid concentration. Various aspects of this phenomenon, along with the transient yellow colour observed in the initial stages of the nitrodeiodination of 4-iodoanisole will be discussed in the next section of this thesis.

A brief study was carried out of the nitrodeiodination of 4-iodophenol. Iodine was released but its appearance was not of

the first order, the latter part of the graph of optical density against time being a straight line with a positive gradient. It was also found that such graphs for the reaction when the nitric acid was 6.4 M, 8.8 M and 11.2 M were essentially superimposable. Further studies of this reaction, possibly changing the solvent since the reaction is extremely slow, are required but it is likely that this unusual behaviour is due to the formation of the dienone:



after attack by 'NO^+' has taken place.

After this work on nitrodeiodination had been completed a paper by Perrin and Skinner[137] appeared which used the nitration of halogenoanisoles to measure ipso partial rate factors, that is, the effect of a substituent on electrophilic attack at the carbon atom to which the substituent is attached. A discussion of this paper, on a subject not previously considered explicitly, is appropriate in view of this study of the mechanism of one of the reactions used.

Using nitric acid in acetic anhydride as the nitrating agent and 4-iodoanisole as substrate, these workers obtained 4-nitroanisole and 2,4-di-iodoanisole but no rearrangement product. This can be easily explained since nitrodeiodination of 2,4-di-iodoanisole to give rearrangement product is much slower than the initial processes and would occur only if the reaction mixture was allowed to stand for some time.

Although specifying the nitrating agent is not crucial to the measurement of ipso factors, it was assumed to be NO_2^+ in the system used, and this is open to question. This species was proposed by Paul[138], but later workers have preferred protonated acetyl nitrate[139,140], and this has been confirmed by some recent MINDO calculations[141]. Hartshorn et al.[142] have reported that the relative reactivities of benzene and toluene towards nitration are very different with nitric acid in acetic anhydride from those obtained with nitrating agents in which the reactive species is known to be NO_2^+, indicating a different mechanism. Also, there is evidence[135] for two distinct pathways in nitration by nitric acid in acetic anhydride, one of which is nitrosation followed by oxidation, and a consideration of this reaction is crucial in any study of the nitration of anisole. Bordwell and Garbisch[139] have shown that the reactivity of anisole towards nitration depends upon the temperature and manner in which the nitric acid and acetic anhydride were mixed and in a more recent study by Eaborn et al.[143] it was found that the ortho:para ratio, for the nitration of anisole, is influenced by the presence of nitrogen oxides. The ortho:para ratio for the nitration of anisole is, therefore, subject to uncertainty. Perrin and Skinner attempted to deal with this by the addition of urea, which removes nitrous acid and so prevents nitrosation, but it is difficult to be certain that this is completely effective. Such doubts were raised by Hoggett et al.[144] and confirmed in a recent study of the nitration of thiophen[145]. The extreme susceptibility of anisole to nitrosation, and the fact that more nitrous acid may be produced autocatalytically, makes the complete eradication of nitrosation, by urea, questionable.

The possibility of even a small amount of nitrosation occurring raises another difficulty. The work in this thesis indicates that deiodination by nitric acid is due to nitrosation rather than nitration, but nitrodeprotonation at the 2-position of a 4-halogenoanisole may not involve preliminary nitrosation. This is exactly the situation occurring in the desilylation of p-tolyltrimethylsilane by nitric acid and acetic anhydride[101]. The carbon-silicon bond is readily cleaved by the nitrosating species present (not specified) but NO_2^+ (or whatever nitrating species is present) appears to leave the carbon-silicon bond intact and nitrates the substrate at the 2-position. Therefore, in comparing the relative reactivities of the 2- and 4-positions in 4-halogenoanisoles towards nitration, it is possible that two different electrophiles are involved. However, the constant value for the product ratio reported by Perrin and Skinner under a variety of conditions argues against this, as the extent of nitrosation should vary from run to run, depending on the amount of nitrogen oxides present. On the other hand, the report of erratic results in kinetic studies could result from some nitrosation due to nitrous acid produced autocatalytically. It is not certain that the presence of urea prevents this complication as reaction of the nitrosating species with halogenoanisole may be faster than the reaction of nitrous acid with urea.

The situation would be less uncertain if it was known that NO_2^+ could effect deiodination, even if with less facility than 'NO^+'. This could be the case. Reaction of 4-iodoanisole with nitronium tetrafluoroborate, where the nitrating species is known to be NO_2^+, in anhydrous acetic acid results mainly in nitration at the 2-position, but some iodine is released and some

4-nitroanisole is obtained. This result is not conclusive since it is known that these nitronium salts sometimes contain nitrosyl salts as impurities, and nitrosyl hexafluorophosphate, a source of NO^+, was shown to rapidly deiodinate 4-iodoanisole under the same conditions. In contrast to this Challis[146] found that, when nitrating anisole, NO_2^+, is at least 10^{14} times more reactive than the nitrosating species and it is striking that this behaviour should be reversed when iodine rather than a proton is displaced. Direct comparison with the results of Perrin and Skinner is not possible as the nitrating agent and solvent are different, but some doubts concerning their determination of ipso factors are removed. The problem remains, however, of deciding whether nitrosation plays a part in the dehalogenation reaction under their conditions. Such doubts must remain until the mechanism of nitration in acetic anhydride is more clearly understood. The measurement of ipso factors by use of some other nitrating agent is required but it is surprisingly difficult to find a powerful one not involving a strong acid, which might cause protodehalogenation, for which the mechanism of reaction is known with certainty[12]. Nitronium salts appear as likely reagents but the problem there, is the possibility of a diffusion-controlled reaction rate. The opposing views on this subject have been given in reviews by Olah[147] and Ridd[148] and, until the matter is fully resolved, the measurement of ipso factors by use of these reagents would be subject to just as much ambiguity as at present. The concept of ipso partial rate factors is important and, as Perrin and Skinner point out, much work needs to be done for an understanding of them to develop.

3. INVESTIGATION OF TRANSIENT INTERMEDIATES INVOLVED IN THE NITRODEIODINATION REACTION

In the kinetic nitrodeiodination of 4-iodoanisole, on mixing the substrates a yellow colour is observed, but this disappears before a normal spectral study can be carried out on it. This colour is also observed when the reaction is carried out using nitrosyl hexafluorophosphate as the nitrosating agent but is not observed when either 2,4-di-iodoanisole or 4-iodo-2-nitroanisole are used as the substrate. It was decided, therefore, to examine the transient species responsible for this colour by means of stopped-flow techniques.

The reaction of 4-iodoanisole in acetic acid with sodium nitrite in nitric acid was monitored, with the aid of a Canterbury SF apparatus, at various wavelengths between 380-490 nm, for the first minute of reaction. The absorbance reached a maximum after about 10s and this must be the point when the species responsible for the yellow colouration is at a maximum concentration. Therefore the absorbance at this time was noted, for each run at various wavelengths was plotted against the relevant wavelength and is shown in Figure 19 (Table 20). Examination of the reaction using 2,4-di-iodoanisole as substrate under the same conditions and by the same technique showed no similar spectral changes.

Studies of the nitrodeiodination reaction in water using perchloric rather than nitric acid were planned, using the water soluble substrate 2-(4-iodophenoxy)ethylsulphonic acid, but, although this compound could be deiodinated, spectral studies were not possible due to the formation of a very intense brown colour which masked the absorption due to iodine at 475 nm. On standing

TABLE 20

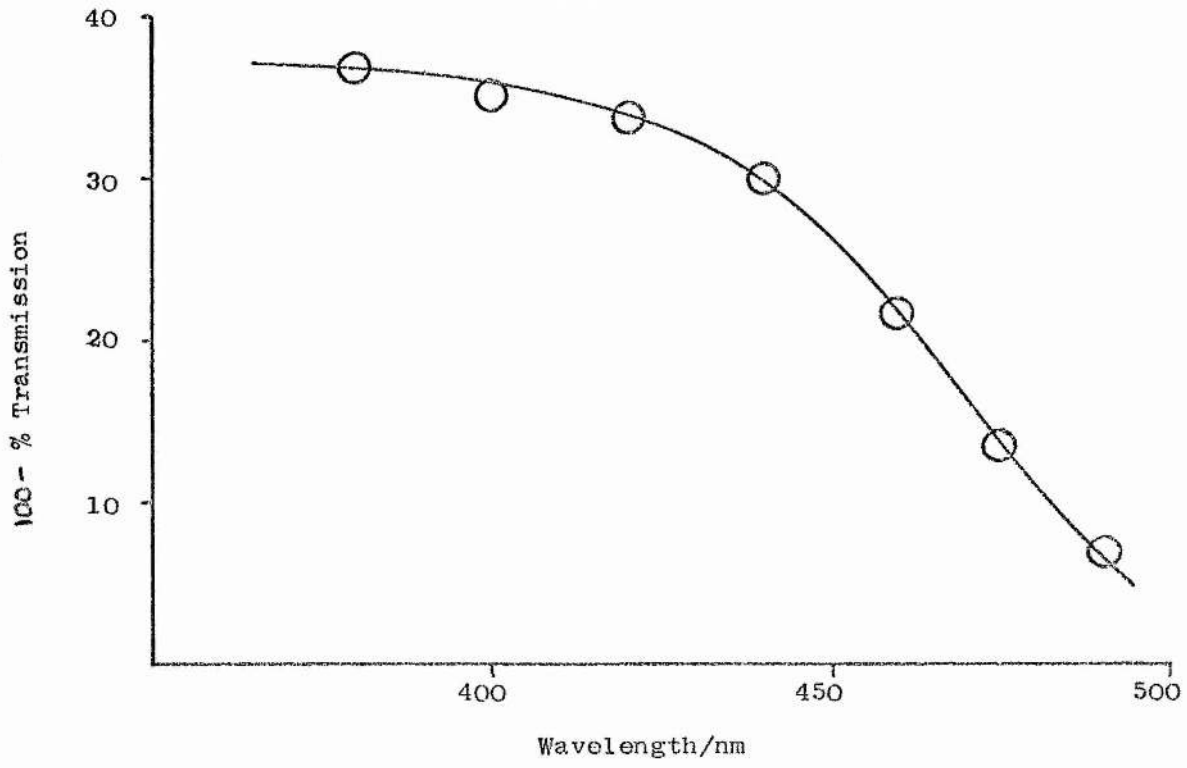
Spectrum of the nitrodeiodination of 4-iodoanisole after 10s at 25°

$[HNO_3]$ = 8.05 M $[NaNO_2]$ = 0.025 M

$[4\text{-Iodo-anisole}]_o = 5.22 \times 10^{-3}$ M

Wavelength/nm	100- % Transmission
380	36.7
400	35.0
420	33.7
440	30.0
460	21.6
475	13.3
490	6.7

Figure 19. Spectrum of the nitrodeiodination of 4-iodoanisole after 10s.



this brown colour slowly disappeared to reveal the iodine peak, but whether the formation of this peak was connected with the disappearance of the brown colour or whether it was already present, but hidden, could not be ascertained. The resulting solution of this reaction was poured into excess sodium hydroxide solution and a yellow colour, which had an ultra-violet/visible spectrum identical with that of an authentic sample of 4-nitrophenol, was observed. This behaviour is paralleled by the nitrosation of anisole in water[149] where the anisole undergoes demethylation giving an end product of 4-nitrophenol. It was decided to decrease the substrate concentration in order that the species responsible for the brown colour might be investigated, in view of its similar, though much slower, behaviour to the yellow colour observed with 4-iodoanisole in acetic acid. The brown colour was monitored at 410 nm, and the graph of change of absorption with time was found to be of similar shape to that observed for the yellow species, but the spectral changes took place in over an hour rather than in less than a minute.

The formation of the species responsible for these changes was found to conform to first order kinetics and the rate of formation was found to be proportional to the concentration of sodium nitrite, see Figure 20 (Table 21) and proportional to the acidity function, h_o, see Figure 21 (Table 22). Similar spectra and behaviour were found using 2-phenoxyethylsulphonic acid as the substrate.

Work by Tedder[150,151], on the direct introduction of a diazonium group into an aromatic nucleus by the use of sodium nitrite and a strong acid, found that these reactions were accompanied by intense red/brown colours and it was proposed[152] that these colours were due to the formation of a complex ion

TABLE 21

Variation of rate of formation of the brown species with concentration of sodium nitrite

[2-(4-Iodophenoxy)ethylsulphonic acid] = 2.76×10^{-3} M

$[HClO_4]$ = 6.48 M Temperature 25°

$[NaNO_2]$/M	10^3 k(obs.)/s^{-1}
0.036	0.98
0.072	1.97
0.108	3.19
0.144	3.91
0.180	4.81

TABLE 22

Variation of rate of formation of the brown species with acidity

[2-(4-Iodophenoxy)ethylsulphonic acid] = 2.76×10^{-3} M

$[NaNO_2]$ = 0.041 M Temperature 25°

$[HNO_3]$/M	h_o(obs)	10^3 k(obs.)/s^{-1}
6.48	148	1.00
7.26	610	2.61
7.92	1930	5.48
8.40	4050	11.18
8.64	6460	16.70

Figure 20. Effect of nitrite on rate of formation of brown species.

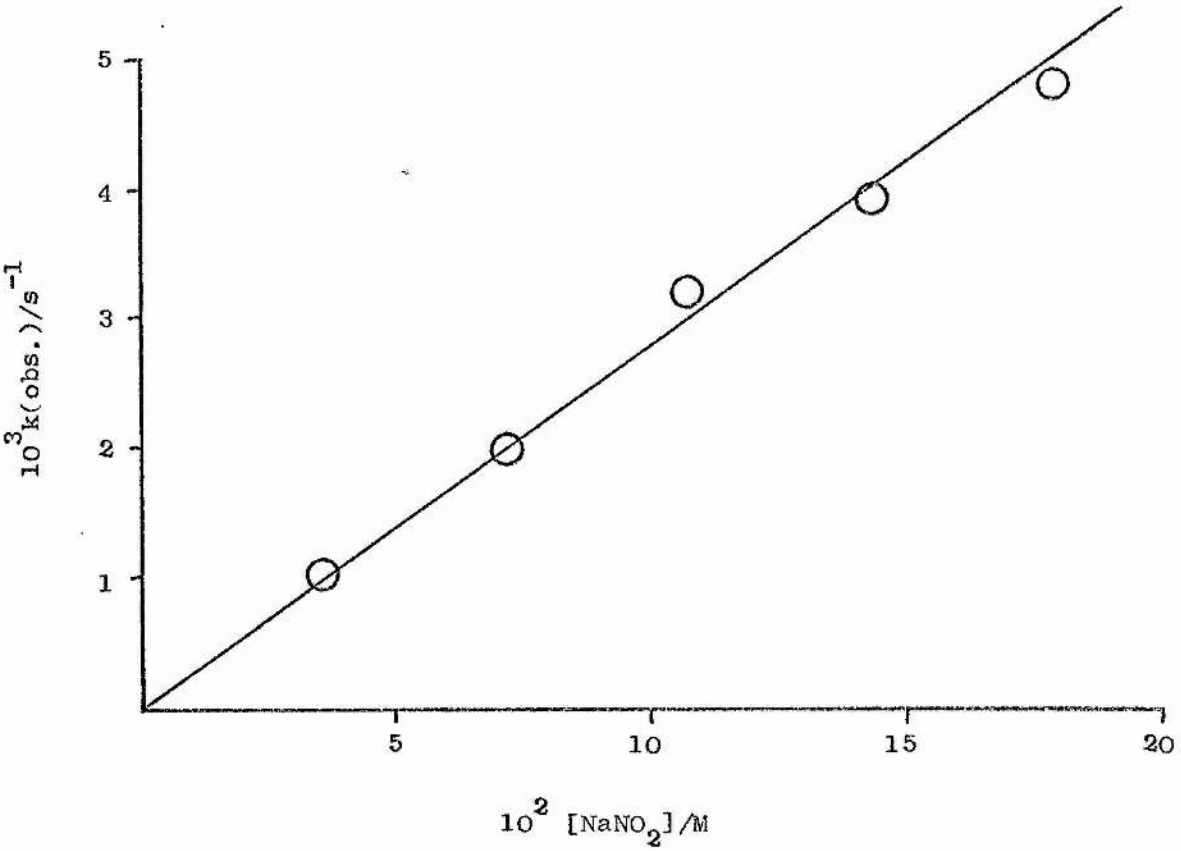
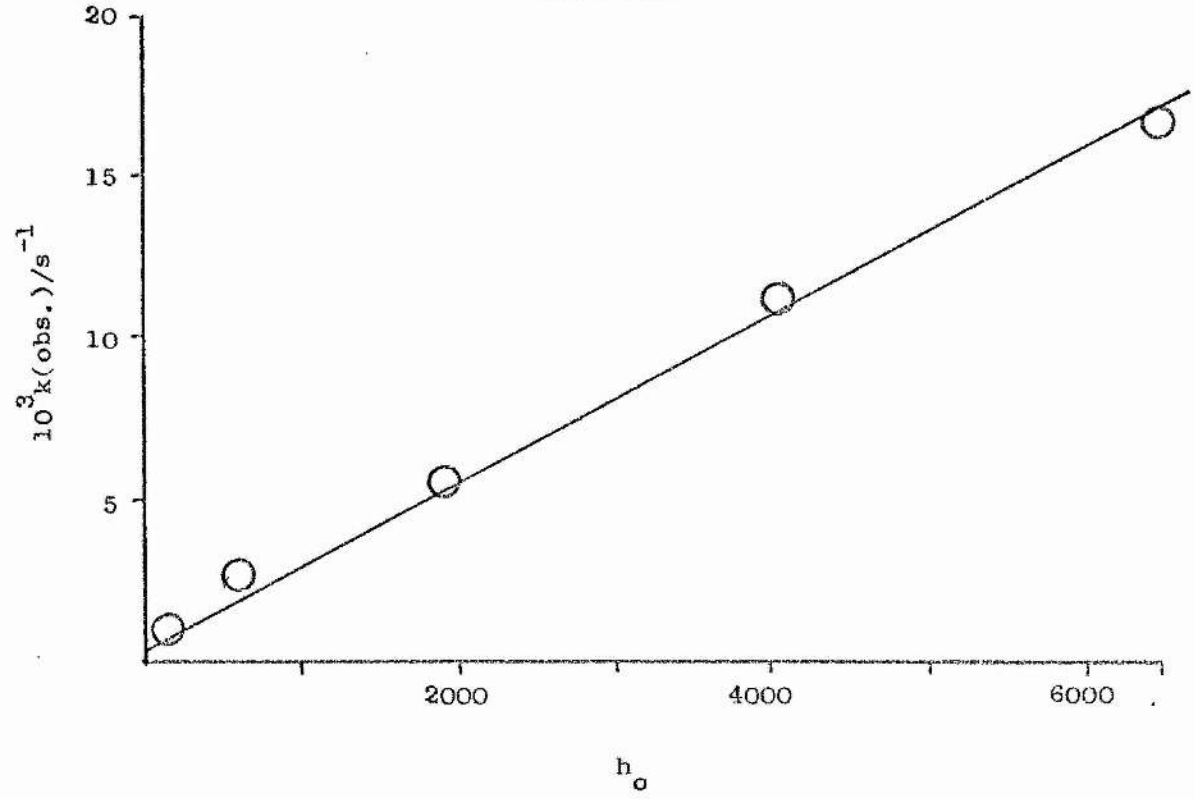
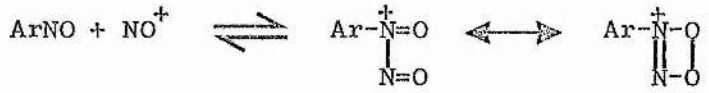


Figure 21. Effect of acidity on rate of formation of the brown species.



from the nitroso-compound, formed from initial nitrosation, and the nitrosonium ion,



similar complexes having been proposed for nitrosoamines[153]. This species would disappear either as the diazo-compound was formed or as the nitroso-compound was oxidised to the nitro-compound. Therefore, it was decided to investigate whether any diazo-compound was formed, under kinetic conditions, with the sulphonic acid as substrate. The reaction was carried out and the resulting mixture was tested with alkaline β-naphthol solution, but no red colouration, characteristic of a diazo-dye, was observed. The β-naphthol test was only positive when concentrated solutions of sodium nitrite in perchloric acid were used directly on the substrate, and even then the red colouration was weak. It was concluded from this that, under kinetic conditions, essentially no diazo-compound is formed and so this sequence of events is not likely to be significant, and is unlikely to be responsible for the observed colour.

Further evidence that the observed spectral changes are not due to initial nitrosation was obtained from a study of the action of sodium nitrite in nitric acid on hexamethylbenzene in acetic acid. This reaction also gives rise to a brown colour but in this case it does not disappear on standing. However, the colour does disappear on addition of urea, which removes nitrous acid, and the recovered material is found to be unchanged hexamethylbenzene. The formation of the brown species increases the solubility of hexamethylbenzene which is essentially insoluble in aqueous perchloric

acid unless sodium nitrite is added, and no brown colour is observed until sodium nitrite is added.

It therefore seems likely that the species is a complex between the substrate and some other entity present in the reaction mixture. The dependence of the rate of formation of the species on sodium nitrite and acidity indicates that the other entity is closely related to the nitrosating species. The fact that the reaction is slow indicates that the complex is not a π-complex, since the formation of these is a one electron process which is essentially instantaneous, and so the species is more likely to be a σ-complex.

There are two possibilities as to the involvement of a complex in the reaction, one is that the complex is an intermediate on the reaction path, the other is that the complex exists in equilibrium with a species which takes part in the reaction. These two possibilities were investigated with the use of an analogue computer. The first possibility

$$A \xrightarrow{k_1} \text{Complex} \xrightarrow{k_2} B$$

was simulated by the circuit shown in Figure 22, and the second possibility

$$\text{Complex} \underset{k_1}{\overset{k_{-1}}{\rightleftharpoons}} A \xrightarrow{k_2} B$$

was simulated by the circuit shown in Figure 24. By the use of the time base, shown in Figure 23, the signal representing the change in concentration, with time, of any of the three species could be displayed by the use of an oscilloscope or a chart recorder. Several such plots for the complex, in both systems, at varying ratios of the rate constants were recorded. It was found that the

Figure 22. Analogue computer circuit for reaction sequence:

$$A \xrightarrow{k_1} \text{Complex(C)} \xrightarrow{k_2} B$$

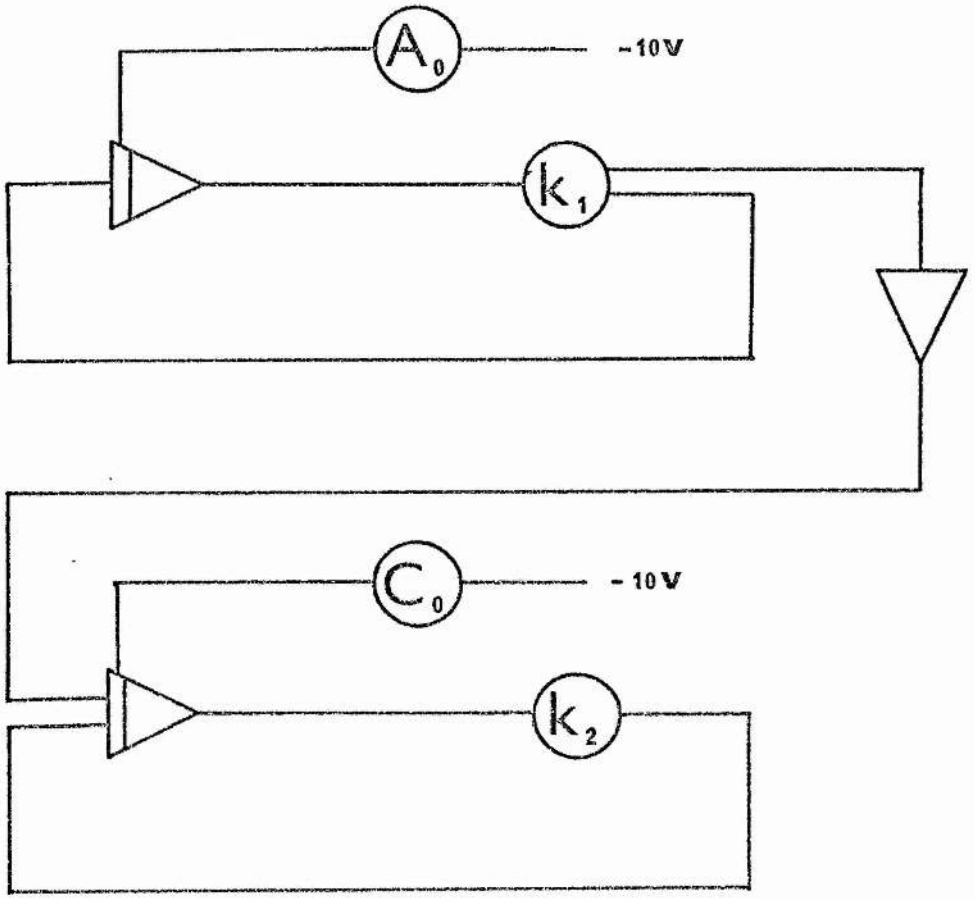
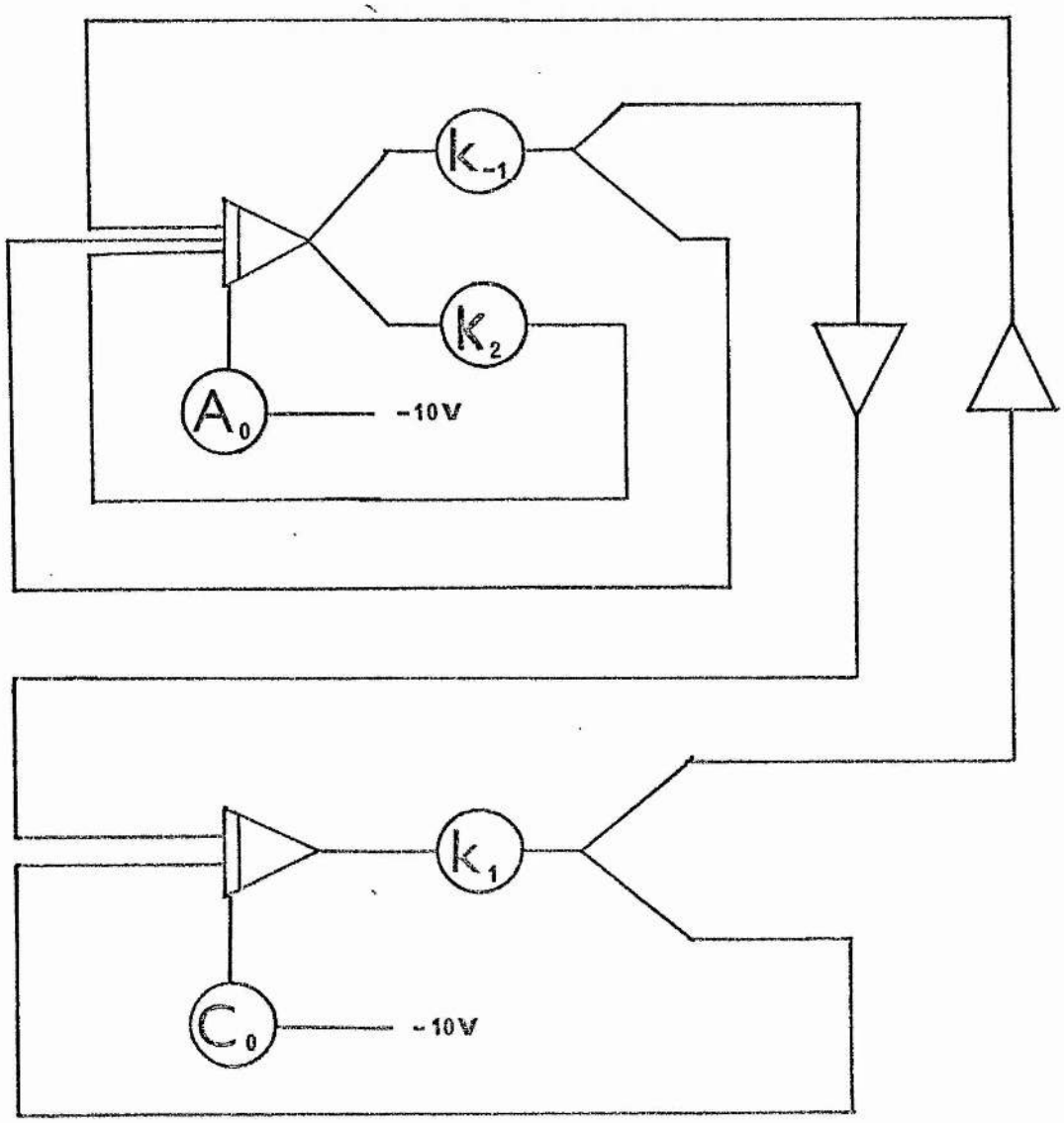


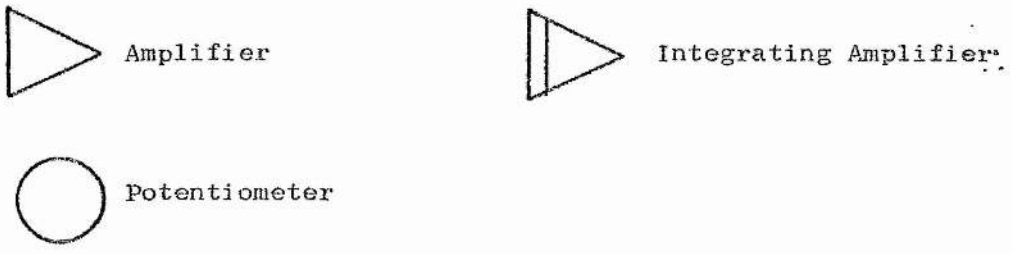
Figure 23. Analogue computer circuit for time base.

Figure 24. Analogue computer circuit for reaction sequence;

$$\text{Complex(C)} \underset{k_1}{\overset{k-1}{\rightleftharpoons}} A \xrightarrow{k_2} B$$

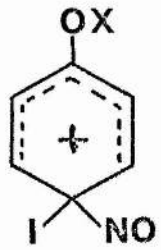


Key for circuit diagrams.



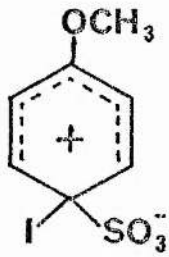
two possibilities are indistinguishable by the shape of the curve obtained since, by correct choice of the ratios of rate constants, both gave a curve similar to that obtained in a kinetic run.

The involvement of the brown species is not clear, and its nature cannot be proposed with a great deal of certainty, but the evidence indicates that it is a σ-complex involving the nitrosating agent and may well be a species of the type



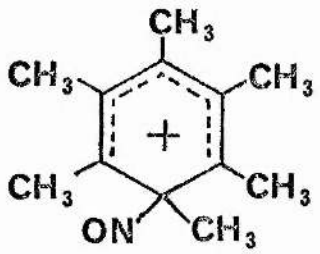
where X is either the ethylsulphonic group or the methoxy group.

Suzuki[56], in a study of the Jacobsen reaction, found that when sulphuric acid was added to 4-iodoanisole an intense brown colour was observed and he concluded that this was due to the analogous complex



A species of the proposed type would be involved in the reaction path and would only be observable when the rate of attack by the nitrosating agent is faster than the loss of iodine, resulting in a build-up of the complex. This may be why the

species is not observed with 2,4-di-iodoanisole and 4-iodo-2-nitroanisole which are more deactivated towards electrophilic attack. Also, the stability of the species in the case of the sulphonic acids may be due to the fact that under the reaction conditions these substrates form phenols and thus stabilisation is possible by the formation of a dienone. Lastly the behaviour of hexamethylbenzene can be explained by the fact that a complex of the type



can be formed but subsequent loss of a methyl group is highly unlikely and so no further reaction takes place, except when urea is added and the complex reverts to hexamethylbenzene.

PART III

EXPERIMENTAL

1. SOURCES, PURIFICATION AND PREPARATION OF MATERIALS

AnalaR acetic anhydride, benzene, iodine, sulphuric acid and toluene were used without further purification.

AnalaR sodium nitrite and urea were dried under vacuum before use.

Laboratory reagent lithium chloride, lithium bromide, lithium, iodide and lithium perchlorate were dried under vacuum before use.

Thallium(III) trifluoroacetate was supplied by Thallium Ltd., Norwich.

Nitronium tetrafluoroborate and nitrosyl hexafluorophosphate were supplied by K and K Laboratories, California.

B.D.H. standard solutions of sodium hydroxide were used.

[^{14}C]-Benzene (5 μCi/m), [^{14}C]-phenol (50 μCi mole^{-1}), and [^{14}C]-toluene (5 μCi/ml) were supplied by The Radiochemical Centre, Amersham.

Deuteriated water with a stated deuterium content of 99.7% was supplied by Koch-Light.

Mesitylene, m-xylene, 2-bromoanisole, nitromethane, trifluoroacetic acid, 2-iodotoluene, 4-iodotoluene, 2-iodoanisole, 3-iodoanisole, thiophen, chlorothiophen and hexane were carefully distilled before use.

Hexa-ethylbenzene, hexamethylbenzene, 4-iodoanisole, 4-nitroanisole, 2-nitroaniline, and 4-nitroaniline were recrystallised twice from ethanol before use.

AnalaR nitric acid was used without further purification and standardised by diluting one hundred times with water and titrating against standard sodium hydroxide solution using phenolphthalein as indicator.

AnalaR acetic acid was used without further purification in

most cases, but when anhydrous acid was required it was purified as follows.

(i) The freezing point of the acid was measured using the normal type of apparatus.

(ii) Taking the freezing point of anhydrous acid as 16.6° it is known that the freezing point is lowered by 0.2° for every 0.1% water present.

e.g. freezing point of acid = 15.6° corresponds to,

0.5% water present = 0.5 g water per 100 g acid.

(iii) The water content of the acid was calculated in this way and an appropriate amount of AnalaR acetic anhydride was added, with chromium trioxide, to remove the water present. The temperature of this mixture was then raised to just below distillation point and maintained there for 30 min., and then the acid was slowly distilled using a splash-head. This purification is based on the method of Orton and Bradfield[154].

Dinitrogen tetroxide[155]: Dried, commercial, lead nitrate was heated strongly in a test-tube contained in a pyrex tube. The water and nitric acid evolved were condensed by a water cooled condenser and the gas was dried by passing it up a drying tower packed with phosphorus pentoxide on glass wool. Dinitrogen tetroxide was condensed and solidified in a flask, surrounded by a Dry Ice-acetone bath, and protected from the atmosphere by a phosphorus pentoxide guard tube. The solid product was colourless, any colour indicating impurities.

2-Iodo-4-nitroanisole: 4-Nitroanisole (10 g) was dissolved in a mixture of acetic acid (100 ml) and nitric acid (15 ml). Sodium nitrite (15 ml of a 0.05 M solution) and iodine (10 g) were added

and the mixture was stirred for 4 days. After pouring into water any excess of iodine was removed by adding sodium bisulphite. The 2-iodo-4-nitroanisole was filtered off and recrystallised from ethanol, m.p. 96° (lit.[2], 96°). Yield = 62%

Required analysis: C = 30.13% H = 2.17% N = 5.02%

Found: C = 30.08% H = 2.18% N = 4.82%

4-Iodo-2-nitroanisole(2): 2-Nitroanisole (7 g) and iodine (9 g) were stirred with nitric acid (14 ml) for 24 h. After pouring into water the excess of iodine was removed by adding sodium bisulphite and the 4-iodo-2-nitroanisole was filtered off and recrystallised from ethanol, m.p. 97° (lit.[2], 98°). Yield = 57%.

Required analysis: C = 30.13% H = 2.17% N = 5.02%

Found: C = 29.93% H = 2.20% N = 5.04%

The identity of the two above isomers was checked by examination of their n.m.r. spectra.

2,4-Dinitroanisole[156]: Anisole (5 g) was warmed with concentrated sulphuric acid (5 ml) until a drop would not turn a drop of water cloudy. After cooling, this mixture was added to nitric acid and sulphuric acid (5 ml of a 50/50 mixture) keeping the temperature below 20°. The mixture was heated gently on a water bath before stirring into cold water from which 2,4-dinitroanisole was filtered off and recrystallised from ethanol, m.p. 94° (lit.[156], 95°). Yield = 43%.

Required analysis: C = 42.43% H = 3.05% N = 14.14%

Found: C = 42.52% H = 3.14% N = 14.05%

2,4-Di-iodoanisole: 2-Iodoanisole (10 g) was dissolved in acetic acid (80 ml) and nitric acid (15 ml). Sodium nitrite (5 ml of a

0.05 M solution) and iodine (7.5 g) were added and the mixture was stirred for 24 h. After pouring into water the excess of iodine was removed by adding sodium bisulphite. The 2,4-di-iodoanisole was filtered off, recrystallised from ethanol, m.p. 68° (lit.[157], 68°). Yield = 65%.

Required analysis: C = 23.36% H = 1.68%

Found: C = 23.33% H = 1.67%

4-Iodo-2,6-dimethylanisole[51]: 2,6-Dimethylanisole (2.44 g) was added to thallium(III) trifluoroacetate (10 g) in trifluoroacetic acid (25 ml) and stirred for 15 min. A solution of potassium iodide (13 g) in water (25 ml) was added and stirred for a further 15 min. After adding sodium bisulphite, and stirring for 15 min, the mixture was basified with 4N sodium hydroxide and diluted with ether. The thallium iodide was removed by filtration and the aqueous layer was extracted with ether. The ether extracts and layer were combined, washed with water, and dried with anhydrous magnesium sulphate. The ether was removed by evaporation, leaving a residue of 4-iodo-2,6-dimethylanisole which was distilled, b.p. 74-76° at 0.4 mm (lit.[158], 87° at 1.0 mm). Yield = 70%.

Required analysis: C = 41.25% H = 4.23%

Found: C = 41.42% H = 4.41%

NOTE: As thallium salts are toxic, this preparation was carried out entirely in a fume cupboard, rubber gloves were worn at all times and a special thallium residue bottle was used.

2-Phenylthiophen[159]: This preparation involves the reaction of 2-lithiothiophen with cyclohexanone and subsequent dehydrogenation of the product with chloranil.

An ethereal solution of 2-lithiothiophen was prepared by adding n-butyl lithium (0.21 moles) - prepared by adding n-butylbromide (82.2 g) gradually to lithium (12 g) in ether (350 ml), keeping the apparatus blown out with nitrogen at all times - to thiophen (26 g) in ether (100 ml) and stirring for 15 min.

This solution was cooled in a Dry Ice-acetone bath, cyclohexanone (29.5 g) was added rapidly, and the mixture left overnight before being hydrolysed by addition of cold hydrochloric acid.

The organic layer was washed with water, dried with anhydrous magnesium sulphate and distilled to give 2-(1-cyclohexenyl)-thiophon boiling between 99-103^{o} (2 mm).

A mixture of chloranil (75 g), 2-(1-cyclohexenyl)-thiophen (25 g) and benzene (250 ml) was refluxed for 24 h, when the product was filtered and the filtrate was extracted with sodium hydroxide (12%) until the extracts were colourless. The benzene layer was washed with water and dried with anhydrous sodium sulphate. The benzene was removed by evaporation and the residue was distilled to give 2-phenylthiophen b.p. 82^{o} (1 mm) which was recrystallised from aqueous methanol, m.p. 35^{o} (lit^{157} 37^{o}). Yield = 25%. The compound was stored in a brown bottle in the refrigerator.

Required analysis: C = 74.9% H = 5.03 %

Found: C = 74.74% H = 5.24%

2-Iodo-5-phenylthiophen 2-Phenylthiophen (1 g) was added to thallium(III) trifluoroacetate (3.4 g) in acetonitrile (8 ml) and stirred for 20 min. A solution of potassium iodide (7.9 g) in water (10 ml) was added and stirred for a further 15 min. After adding sodium bisulphite and stirring for 15 min, the mixture was

made basic with 4N sodium hydroxide and diluted with ether. The precipitated thallium iodide was removed by filtration and the aqueous layer was extracted with ether. The ether extracts and layer were combined, washed with water, dried with anhydrous magnesium sulphate and the ether evaporated, leaving a residue of 2-iodo-5-phenylthiophen which was recrystallised from ethanol, m.p. 81° (lit.[160] 81.5°). Yield = 75%.

Required analysis: C = 41.98% H = 2.47%

Found: C = 42.19% H = 2.55%

2-Deutero-5-phenylthiophen: Throughout this preparation dry nitrogen was bubbled through the reaction solution.

A solution of 2-phenylthiophen (3.5 g) in dry ether (50 ml) was cooled to 0°. A solution of butyl lithium in hexane (15 ml of a 15% solution) was added to this with stirring over 30 min, keeping the temperature at 0°. After stirring the solution for a further 30 min deuteriated water (5 ml) was added, keeping the temperature below 20°, and then stirred for 90 min. The solution was dried with anhydrous sodium sulphate, the ether removed by evaporation and the residue was dissolved in ethanol and boiled with activated charcoal. The mixture was filtered, concentrated and allowed to crystallise. Recrystallisation from ethanol gave 2-deutero-5-phenyl thiophen. The presence of the deuterium was confirmed by n.m.r.

4-Iodophenol[161]: 4-Aminophenol (54.5 g) was dissolved in a mixture of water (250 ml), concentrated sulphuric acid (32.5 ml) and crushed ice (250 ml). Throughout the preparation dry nitrogen was bubbled through the reaction mixture. The mixture was stirred and a solution of sodium nitrite (36 g) in water (75 ml) was added over 1 h, keeping the temperature at 0°. After stirring for a

further 20 min, sulphuric acid (10 ml) was added and the cold solution was poured into an ice-cold solution of potassium iodide (100 g) in water (100 ml) and stirred. After 5 min copper metal (1 g) was added and the solution was warmed slowly to 75° and maintained at that temperature until nitrogen evolution had ceased. The mixture was cooled and extracted with chloroform, the extracts being washed with dilute sodium bisulphite solution and dried with anhydrous magnesium sulphate. The chloroform was evaporated and the residue was extracted with refluxing 80-100° petroleum ether from which 4-iodophenol crystallised, m.p. 92° (lit.[161] 94°). Yield = 53%.

Required analysis: C = 32.76% H = 2.29%

Found: C = 32.69% H = 2.32%

Sodium salt of 2-(4-iodophenoxy)-ethylsulphonic acid[162]: This preparation involves the reaction of sodium sulphite with 1-(2-bromo-ethoxy)-4-iodobenzene.

A solution of 4-iodophenol (40 g) in ethanol (500 ml) was refluxed for 4 h with 1,2-dibromo-ethane (40 ml) and sodium (5 g). This mixture was poured into water to give a white precipitate which was filtered off and recrystallised from ethanol to give 1-(2-bromo-ethoxy)-4-iodobenzene. Yield = 30%.

A solution of 1-(2-bromo-ethoxy)-4-iodobenzene (20 g) and sodium sulphite heptahydrate (16 g) in water (25 ml) was refluxed for 30 h. The white precipitate which formed was filtered off, when the solution had been cooled, and recrystallised from ethanol, then water to give the sodium salt of 2-(4-iodophenoxy) ethylsulphonic acid. Yield = 15%.

Required analysis: C = 27.45% H = 2.30%

Found: C = 27.31% H = 2.32%

Sodium salt of 2-phenoxy-ethylsulphonic acid[162]: This preparation was carried out in an analogous method to the preparation of the sodium salt of 2-(4-iodophenoxy)ethylsulphonic acid starting with phenol instead of iodophenol. The product was found to have one water of crystallisation associated with it. Yield = 10%.

Required analysis: C = 39.67% H = 4.58%

Found: C = 39.61% H = 4.66%

1,4-Di-iodobenzene[19]: Nitric acid (25 ml) was added in portions (5 ml) at intervals of 1 h to a mixture iodobenzene (25 ml) and iodine (30 g). Some carbon tetrachloride was added to the mixture, to prevent the iodine subliming in subsequent heating, and the mixture was heated for 6 h. The reaction mixture was washed first with dilute sodium bicarbonate solution and then water, and then steam distilled to remove iodine and oily products. The residue was recrystallised from ethanol to give 1,4-di-iodobenzene, m.p. 128° (lit[157] 129°). Yield = 56%.

Required analysis: C = 21.84% H = 1.22%

Found: C = 21.77% H = 1.23%

2-Iodomesitylene[51]: Mesitylene (3.24 g) was added to thallium(III) trifluoroacetate (15 g) in trifluoroacetic acid (35 ml) and stirred for 15 min. A solution of potassium iodide (20 g) in water (35 ml) was added and the mixture stirred for a further 15 min. After basifying with 4 M sodium hydroxide, the solution was filtered and extracted with ether. The extract was washed with water, dried with anhydrous magnesium sulphate, and the ether removed by evaporation. The residue was recrystallised to give 2-iodomesitylene, m.p. 30° (lit.[157] 30°). Yield = 70%.

Required analysis: C = 43.83% H = 4.51

Found: C = 43.86% H = 4.52%

2-Nitromesitylene[163]: A solution of mesitylene (10 g) in acetic anhydride (14 ml) was cooled to 5°. A mixture of fuming nitric acid (5.1 ml), acetic acid (5 ml) and acetic anhydride (4.6 ml) [see Appendix 4] was added during 40 min, keeping the temperature below 20°. The mixture was allowed to stand at room temperature for 2 h and then heated, with shaking, to 50° on a water bath. After the mixture was cooled and poured into iced water (200 ml), sodium chloride (10 g) was added, and the mixture was filtered. The filtrate was extracted with ether and the residue was dissolved in ether. The ether solution was washed with 10% sodium hydroxide until the washings were alkaline, dried with anhydrous magnesium sulphate and the ether removed by evaporation. The residue was recrystallised from ethanol to give 2-nitromesitylene m.p. 42° (lit.[163] 43°). Yield = 63%.

Required analysis: C = 65.44% H = 6.71% N = 8.48%

Found: C = 65.32% H = 6.81% N = 8.47%

2-Iodo-4-nitromesitylene: A solution of 2-iodomesitylene (1 g) in acetic anhydride (3 ml) was cooled to 5°. A mixture of fuming nitric acid (0.27 ml), acetic acid (0.25 ml) and acetic anhydride (0.23 ml) [see Appendix 4] was added keeping the temperature below 20°, and the mixture was stirred at room temperature for 6 h. After heating at 50° for 2 min the mixture was worked up as described for 2-nitromesitylene, giving 2-iodo-4-nitromesitylene which was recrystallised from ethanol, m.p. 96° (lit.[164] 96°). Yield = 62%.

Required analysis: C = 37.14% H = 3.46% N = 4.81%

Found: C = 37.00% H = 3.37% N = 4.78%

Anhydrous nitric acid[165]: Anhydrous nitric acid was distilled, in diffuse sunlight, from a mixture of equal volumes of AnalaR

fuming nitric acid and AnalaR sulphuric acid, chilled before mixing, as a colourless liquid b.p. 18° (13 mm) and stored in a dark bottle in a refrigerator.

[^{14}C]-Anisole[166]: A solution of [^{14}C]-phenol (9.4 g) in 10% sodium hydroxide (50 ml) and dimethylsulphate (12 ml) was stirred vigorously for 30 min and then heated slowly to 100° on a water bath and maintained at that temperature for a further 30 min. The mixture was steam distilled to give [^{14}C]-anisole. Yield = 85%.

[^{14}C]-4-Iodo-anisole[167]: A solution of [^{14}C]-anisole (9.6 g) in dry carbon tetrachloride (50 ml) was stirred rapidly with yellow mercuric oxide (6g), and iodine (25 g) was added gradually. Further quantities of mercuric oxide (5 g and 3 g) were added during the course of the reaction. The mixture was kept at 50° for 4 h while dry air was bubbled through it. After the mixture was filtered the residue was washed with hot carbon tetrachloride. The washings and the organic layer of the filtrate were washed with sodium bisulphite solution, water, and dried with anhydrous magnesium sulphate. The carbon tetrachloride was removed by evaporation and the residue was recrystallised from methanol to give [^{14}C]-4-iodo-anisole which had m.p. 67° (lit.[167], 68°). Yield = 57%.

[^{14}C]-4-Nitrophenol[168]: [^{14}C]-Phenol (10 g) in water (2 ml) was added to a solution of sodium nitrate (15 g) in sulphuric acid (14 ml) and water (40 ml) cooled in ice, keeping the temperature below 20°, and allowed to stand for 1 h with frequent shaking. After the mother liquor had been decanted, the residue was washed several times with water until the washings were neutral. The

mixture was steam distilled until no more [^{14}C]-2-nitrophenol passed over. The residue was cooled in ice and the crude [^{14}C]-4-nitrophenol was filtered off, boiled with 2% hydrochloric acid (100 ml) and activated charcoal (1 g) for 10 min, filtered and the filtrate allowed to crystallise overnight, giving pure [^{14}C]-4-nitrophenol which was removed by filtration. Yield = 20%.

[^{14}C]-4-Nitroanisole[166]: [^{14}C]-4-Nitrophenol (10 g) was ground with anhydrous potassium carbonate (20 g) and suspended in xylene (50 ml). The suspension was refluxed for 4 h, adding dimethylsulphate (12 ml) proportionwise. The mixture was steam distilled to give xylene followed by [^{14}C]-4-nitroanisole which was filtered off and dried. M.p. 53° (lit.[166], 54°). Yield = 60%.

[^{14}C]-Iodobenzene[18]: Fuming nitric acid (15 ml) was added during 90 min to [^{14}C] benzene (20 g) and iodine (18 g) at 50° and then refluxed for 15 min. The lower oily layer was separated, when cool, mixed with an equal volume of 10% sodium hydroxide, and steam distilled until no more oil passed over. The distillate was stirred with hydrochloric acid (1 ml), water (16 ml) and iron filings (12 g) to remove nitro-compounds. The mixture was filtered, rendered distinctly acid and steam distilled, the distillate being distilled and the fraction boiling at about 185° was purified by column chromatography to give [^{14}C]-iodobenzene. Yield = 56%.

[^{14}C]-2,4-Di-iodoanisole[26]: A mixture of [^{14}C]-anisole (6 g), acetic acid (40 ml), water (10 ml), iodic acid (2.1 g), iodine (5.1 g), sulphuric acid (0.7 ml) and carbon tetrachloride (15 ml) were heated, with stirring, at 40° for 2 h, when further quantities of iodic

acid (2.1 g) and iodine (5.1 g) were added and the mixture was heated for a further 2 h at 60°. The mixture was heated at 75° until all the iodine had disappeared, then poured into water (300 ml) and extracted with carbon tetrachloride. The extracts were washed with sodium carbonate solution and water, dried with anhydrous sodium sulphate and the carbon tetrachloride removed by evaporation. The residue was recrystallised from ethanol giving [^{14}C]-2,4-di-iodoanisole, m.p. 68° (lit.[26], 69°). Yield = 59%.

2. PRODUCT ANALYSES

Analysis of the products of iodination of toluene under kinetic conditions.

Iodine (0.276 g) was added to a mixture of [^{14}C]-toluene (2 ml) nitric acid (5 ml), 0.05 M sodium nitrite (5 ml) and acetic acid (38 ml) and stirred for 48 h , when the brown colour due to iodine had disappeared. After pouring into water (200 ml), unlabelled 4-iodotoluene (4.059 g) and 2-iodotoluene (6.5644 g) were added. The mixture was extracted with ether and the extracts washed with dilute sodium bicarbonate solution and water, and dried with anhydrous magnesium sulphate. The ether was removed by evaporation and the residue was distilled, the fraction distilling at about 210^{o} being collected.

It was intended to separate the two isomers by fractional crystallisation, but, although the 4-iodotoluene separated out as crystals when cooled in an ice-salt bath, it melted before it could be filtered off. Therefore it was decided to examine the isomers as a mixture and they were redistilled to purify. The mixture was then examined for radioactivity by means of a Beckman LS100 Liquid Scintillation Counter with a Fluoralloy cocktail in toluene.

0.0031 g iodotoluenes had a count of 642 (mean).

If all the iodine present entered the toluene nucleus, the count for this quantity of iodotoluenes would be 690.

Therefore almost all the iodine present initially is converted into mono-iodotoluenes, under these conditions.

Product analysis of the nitrodeiodination of 4-iodoanisole under kinetic conditions.

A solution of sodium nitrite (1 g) in nitric acid (20 ml) was added to a solution of 4-iodoanisole (1 g) in acetic acid (20 ml)

and stirred for 72 h. After pouring into water (100 ml) the excess iodine was removed by adding sodium bisulphite. The mixture was filtered and the residue was recrystallised from ethanol to give 2-iodo-4-nitroanisole, m.p. 96° (lit. (2), 96°) which was identified by n.m.r. and I.R.

Required analysis: C = 30.13% H = 2.17% N = 5.02%

Found: C = 30.24% H = 2.22% N = 5.10%

Product analysis of the nitrodeiodination of 4-iodo-2-nitroanisole.

A solution of 4-iodo-2-nitroanisole (1 g) and sodium nitrite (1 g) in nitric acid (25 ml) was stirred for 72 h. After pouring into water (100 ml) the excess iodine was removed by addition of sodium bisulphite and the mixture was filtered. The residue was recrystallised from ethanol to give 2,4-dinitroanisole, m.p. 94° (lit.(156), 95°).

Required analysis: C = 42.43% H = 3.05% N = 14.14%

Found: C = 42.40% H = 3.11% N = 14.03%

Product analysis of the iodination of 2-phenylthiophen, under kinetic conditions.

2-Phenylthiophen (0.1 g) and iodine (0.006 g) were dissolved in acetic acid (18 ml) and 0.05 M sodium nitrite (2 ml) and nitric acid (0.2 ml) were added. After stirring for 10 min, the mixture was poured into dilute sodium hydroxide and then extracted with ether. The ether extract was washed with water and dried with anhydrous sodium sulphate, and then concentrated by evaporation. A thin layer chromatagram was run on a spot of this solution using a carbon tetrachloride/benzene mixture as eluent. The main spot from the experimental solution was found to have an identical Rf. value to authentic 2-iodo-5-phenylthiophen.

Radio-isotopic study of the nitrodeiodination of 4-iodoanisole.

Sodium nitrite (0.35 g) in nitric acid (100 ml) was added to [^{14}C]4-iodoanisole (0.998 g) in acetic acid (100 ml), shaken and divided into two equal portions. After 35s, one portion (A) was poured into water (150 ml), with inactive 2,4-di-iodoanisole (3.005 g) present, and the other portion (B) was poured into water (150 ml), with inactive 4-nitroanisole (3.004 g) present.

Each mixture was extracted with ether (3 x 50 ml), the extracts being washed with water, dilute sodium carbonate solution, sodium bisulphite solution (to remove excess iodine) and finally water. After being dried with anhydrous sodium sulphate the ether was removed by evaporation and the residues were recrystallised from ethanol to constant activity.

Further runs were carried out under the same conditions using less 4-iodoanisole (0.504 g), and, after 30 min, one portion (C) of this mixture was poured into water (150 ml), with inactive 4-nitroanisole (1.503 g) present, and the other (D) into water (150 ml), with inactive 2-iodo-4-nitroanisole (1.37 g) present.

These mixtures were worked up in an identical method to portions A and B.

The experiment was also carried out, adding and retrieving 4-nitrotoluene to the quenched reaction mixture. This was carried out to check the experimental method, since this compound is highly unlikely to take any part in the reaction and since, after recrystallisation it gave no significant count, the method is accurate for determining which compounds take part in the reaction.

The activity of samples was measured on a Beckman LS100 Liquid Scintillation Counter using a Fluoralloy cocktail in toluene.

The results from these experiments were analysed with the aid of the computer programme APRADC, (see Appendix 5).

Counts min^{-1} mol^{-1}, added 4-iodoanisole = 1.92×10^{8}

A. Counts min^{-1} mol^{-1}, retrieved 2,4-di-iodoanisole = 1.78×10^{7}

B. Counts min^{-1} mol^{-1}, retrieved 4-nitroanisole = 8.17×10^{6}

C. Counts min^{-1} mol^{-1}, retrieved 4-nitroanisole = 8.58×10^{6}

D. Counts min^{-1} mol^{-1}, retrieved 2-iodo-4-nitroanisole = 7.83×10^{6}

Determination of the isomer ratio of the products of the nitrodeiodination of 2,4-di-iodoanisole.

A solution of sodium nitrite (0,35 g) in nitric acid (100 ml) was added with stirring to a solution of [^{14}C]-2,4-di-iodoanisole in acetic acid (100 ml). After 30 min the solution was divided into two equal portions, one (A) was added to a suspension of inactive 2-iodo-4-nitroanisole (1.475 g) in water (150 ml) and the other (B) was added to a suspension of inactive 4-iodo-2-nitroanisole (2.803 g) in water (150 ml).

Each portion was worked up in an identical method to that in the above experiment.

A. Counts min^{-1} mol^{-1}, retrieved 2-iodo-4-nitroanisole = 3.05×10^{7}

B. Counts min^{-1} mol^{-1}, retrieved 4-iodo-2-nitroanisole = 1.67×10^{6}

These results were analysed with the aid of the computer programme APRADC, (see Appendix 5).

Nitro-deiodination in the 2-position = 8%.

Nitro-deiodination in the 4-position = 92%.

Investigation of the involvement of 4-nitroanisole in the nitrodeiodination of 4-iodoanisole.

A solution of sodium nitrite (0.35 g) in nitric acid (100 ml) was added with stirring to a solution of 4-iodoanisole (0.988 g) and [^{14}C]4-nitroanisole (0.306 g) in acetic acid (100 ml). The

solution was divided into two equal volumes and after 30 min one portion (A) was added to a suspension of inactive 2-iodo-4-nitroanisole (1.013 g) in water (150 ml). After 36 h the second portion (B) was added to a suspension of inactive 2-iodo-4-nitroanisole (1.014 g) in water (150 ml).

Each portion was worked up in an identical method to that in the above experiment.

A. Counts min^{-1} mol^{-1}, retrieved 2-iodo-4-nitroanisole = 4.47×10^4

B. Counts min^{-1} mol^{-1}, retrieved 2-iodo-4-nitroanisole = 6.70×10^6

Since relatively large quantities of [^{14}C]4-nitroanisole were used in this experiment it is not possible to draw precise quantitative conclusions from these results. However, it is obvious that after 30 min very little of the [^{14}C]4-nitroanisole has been incorporated into the produced 2-iodo-4-nitro-anisole, whereas after 72 h, when the reaction is complete, a considerable amount has been incorporated.

Comparison of the action of sodium nitrite in nitric acid on 2-, 3-, and 4-iodoanisole.

The following method was followed for 2-iodoanisole (A), 3-iodoanisole (B), and 4-iodoanisole (C).

A solution of sodium nitrite (0.17 g) in nitric acid (50 ml) was added to the iodoanisole isomer (4.5 g) in acetic acid (50 ml). After 72 h the mixture was poured into water (150 ml) and treated with sodium bisulphite to remove free iodine.

Portions A and C were filtered and the residues were recrystallised from ethanol to give, in both cases, 2-iodo-4-nitroanisole which was identified by n.m.r. and infra-red spectrometry.

Required analysis: C = 30.13% H = 2.17% N = 5.02%

Found for A: C = 29.97% H = 2.20% N = 5.04%

Found for C: C = 30.01% H = 2.16% N = 4.95%

Portion B underwent a number of colour changes and a precipitate formed, on addition to water (150 ml) the precipitate dissolved. This solution was extracted with ether and the extracts were washed, with sodium bisulphite solution, to remove free iodine, with water and dried with anhydrous sodium sulphate. The ether was removed by evaporation and the residue was recrystallised from ethanol to give compound X.

A further experiment was carried out involving a solution of 3-iodoanisole (2 g) in acetic acid (25 ml) to which was added a solution of sodium nitrite (0.08 g) in nitric acid (25 ml). After 1h this solution was added to water (75 ml) and worked as described above, except that the residue was passed down a silica gel column using carbon tetrachloride followed by benzene as eluents.

Several (about 7) coloured bands were observed on the column and the main fraction was identified as 3-iodo-4-nitroanisole. Compound X was also isolated in lower yield than the previous experiment.

Compound X was identified as 3,6-di-iodo-4-nitroanisole by n.m.r., mass spectrum and elemental analysis.

Required analysis: C = 20.74% H = 1.23% N = 3.46% I = 62.71%

Found: C = 20.85% H = 1.30% N = 3.43% I = 62.82%

Reaction of 4-iodoanisole with nitronium tetrafluoroborate

The nitronium salt (3 g) was added to 4-iodoanisole (2 g) in anhydrous acetic acid (100 ml) and stirred for 5 h. After being poured into water (250 ml) the mixture was extracted with ether. The ether extract was washed with water, sodium carbonate solution, sodium bisulphite solution, to remove free iodine, and water, and dried with anhydrous magnesium sulphate. The ether was removed by evaporation and the residue was recrystallised from ethanol. The

main product was identified as 4-iodo-2-nitroanisole by n.m.r. m.p. 96° (lit (2), 96°).

Required analysis: C = 30.13% H = 2.17% N = 5.02%

Found: C = 30.19% H = 2.23% N = 4.91%

A small quantity of another product was obtained which had an infra-red spectrum identical with that of 4-nitroanisole.

Reaction of 4-iodoanisole with nitrosyl hexafluorophosphate.

A solution of the nitrosyl salt (0.1 g) in acetic acid (5 ml) was added to a solution of 4-iodoanisole (0.014 g) in acetic acid (5 ml) and the visible spectrum of the mixture was recorded, by the use of a Unicam SP 800 spectrophotometer, at intervals of 5 min for a period of 30 min.

The peak due to free iodine at 475 nm reached a maximum and did not decrease afterwards. The peak height corresponded to the release of half of the iodine originally present in the 4-iodoanisole.

Comparison of the products of nitration of 2-iodomesitylene in the presence of absence of added sodium nitrite.

(A). 2-Iodomesitylene (25 mg) was dissolved in nitromethane (40 ml) and cooled to 0°. To this was added a mixture of 90% nitric acid (7.5 ml), made up from proper amounts of AnalaR 70% nitric acid and anhydrous nitric acid, treated with urea, and nitromethane (2.5 ml), and the solution was stirred at 0°. An aliquot (I) of 10 ml was removed after 3.5 h and a second (II) of 20 ml after 6.5 h. Each aliquot was poured into water (30 ml) and ammonia was added until the mixture was homogeneous. This mixture was extracted with hexane (3 x 20 ml), the hexane extract was washed with water until the washings were neutral, dried with

anhydrous magnesium sulphate and the solvent removed by evaporation.

(B). The above experiment was repeated with the addition of sodium nitrite (75 mg).

The four residues obtained in the nitration experiments were dissolved in hexane and analysed by GLC (Pye 104).

Column: 10% APL.

Temperature: 195°.

Gas control settings: Nitrogen (80); Hydrogen (43); Oxygen (90).

Authentic samples of 2-iodomesitylene, 2-nitromesitylene and 2-iodo-4-nitromesitylene in hexane were run on the above column, separately and as a mixture as a calibration experiment. The compounds were eluted from the column in the order, hexane, 2-nitromesitylene, 2-iodomesitylene, 2-iodo-4-nitromesitylene.

The products from experiments (A) and (B) were then examined on the same column. So little reaction had occurred in (I) that no useful conclusions could be drawn. However, the amount of 2-nitromesitylene in (BII) was fifteen times as much as that in (AII), clearly indicating that addition of sodium nitrite greatly increases the amount of nitrodeiodination.

Investigation of the reaction of hexamethylbenzene with sodium nitrite and perchloric acid.

Hexamethylbenzene (0.5 g) was added to a solution of sodium nitrite (1 g) in water (10 ml) and perchloric acid (15 ml), and stirred for 10 min. During this time the hexamethylbenzene, insoluble in aqueous perchloric acid only, dissolved to give a brown solution which was filtered. The filtrate was treated with urea, when the solution became colourless and a white precipitate formed. This precipitate was filtered off, washed with water, and dried.

The solid was found to have an I.R. identical to that of authentic hexamethylbenzene, and its identity was confirmed by a mixed melting point with hexamethylbenzene.

Nitration of 1,4-di-iodobenzene by nitric acid and acetic anhydride

A mixture of anhydrous nitric acid (2.6 ml) and acetic anhydride (5 ml) [see Appendix 4] was added to a solution of 1,4-di-iodobenzene (6 g) in nitromethane (20 ml). After 22h the reaction mixture was poured into ice and left overnight. The solid product was filtered off, treated with sodium bisulphite solution to remove the free iodine and recrystallised from ethanol to give 1-iodo-4-nitrobenzene, m.p. 172°(lit (165), 174°). Yield = 45%

Required analysis: C = 28.94% H = 1.62% N = 5.62%

Found: C = 28.95% H = 1.69% N = 5.80%.

Investigation of the possibility of the iodination of benzene during the competitive nitration of iodobenzene

A mixture of anhydrous nitric acid (1.58 ml) and acetic anhydride (3.53 ml) diluted with nitromethane (6 ml), [see Appendix 4] was added, gradually, to a solution of [^{14}C]-benzene (3.9 g) and iodobenzene (10.2 g) in nitromethane (20 ml). After 50 min the mixture was poured onto ice (400 mg) and left for 3 days, when it was made alkaline with 40% sodium hydroxide. This mixture was extracted with ether and the extracts were washed with water and dried with anhydrous magnesium sulphate.

The ether was removed by evaporation and the residue was distilled to give iodobenzene, b.p. 188°, and nitrobenzene, b.p. 210°, which were purified by column chromatography. The residue from the distillation was recrystallised from ethanol to give 1-iodo-4-nitrobenzene, m.p. 173°. All three compounds were

examined for radioactivity by means of a Beckman LS100 Liquid Scintillation Counter using a Fluoralloy cocktail in toluene. Both the iodobenzene and nitrobenzene were found to be essentially inactive, while the 1-iodo-4-nitrobenzene was active.

Determination of the amount of nitrobenzene formed during the nitration of iodobenzene.

The above experiment was repeated starting with [^{14}C]-iodobenzene instead of [^{14}C]-benzene and unlabelled iodobenzene. After the reaction mixture had been poured onto ice and left, nitrobenzene (15.2 g) was stirred into the mixture which was then made alkaline and extracted with ether. The extract was washed with water, dried with anhydrous magnesium sulphate and the ether removed by evaporation. The residue was distilled and the fraction boiling at about 210^{o} was collected and purified by column chromatography to give nitrobenzene. This product was examined for activity by means of a Beckmann LS100 Liquid Scintillation Counter using a Fluoralloy cocktail in toluene.

Counts min^{-1} mol^{-1} iodobenzene = 6.06×10^{7}

Counts min^{-1} mol^{-1} retrieved nitrobenzene = 3.06×10^{6}

3. DETERMINATION OF THE MOLAR EXTINCTION COEFFICIENT, AND EQUILIBRIUM CONSTANT FOR THE FORMATION, OF THE IODINE-M-XYLENE CHARGE TRANSFER COMPLEX.

$$ArH + I_2 \rightleftharpoons ArH.I_2$$

$$K = \frac{[ArH.I_2]}{[ArH][I_2]}$$

A series of acetic acid solutions of iodine (0.0028 M), and varying concentrations of m-xylene were prepared at 25°. The optical densities of these solutions at the complex absorption maximum (320 nm) were determined, using, as a blank, an iodine free solution of m-xylene in acetic acid of the same concentration as that of the solution under measurement, by the use of a Unicam SP 500 spectrophotometer, using 10 mm spectrophotometer cells in a thermostatted cell holder. The concentration of iodine was chosen so that the optical densities of the solutions fell between the values of 1,8 and 0.25. All optical densities were corrected for slight absorption due to free iodine.

This method is based on that of Andrews and Keefer[130].

Using the equation:

$$\frac{[I_2] \times l}{O.D.} = \frac{1}{KxE} \times \frac{1}{[m\text{-xylene}]} + \frac{1}{E}$$

a plot of 1/[m-xylene] against 1/O.D. will give, intercept = $1/(E \times [I_2])$ and gradient = $1/K \times E \times [I_2])$ where E is the molar extinction coefficient, K is the equilibrium constant and l is the path length in cm.

From the plot, see Figure 25 (Table 23),

Intercept = 0.11 Gradient = 2.77

$\therefore$ $\underline{E = 3.29 \times 10^{3}}$ $\underline{K = 4.0 \times 10^{-2}\ 1\ mol^{-1}}$

TABLE 23

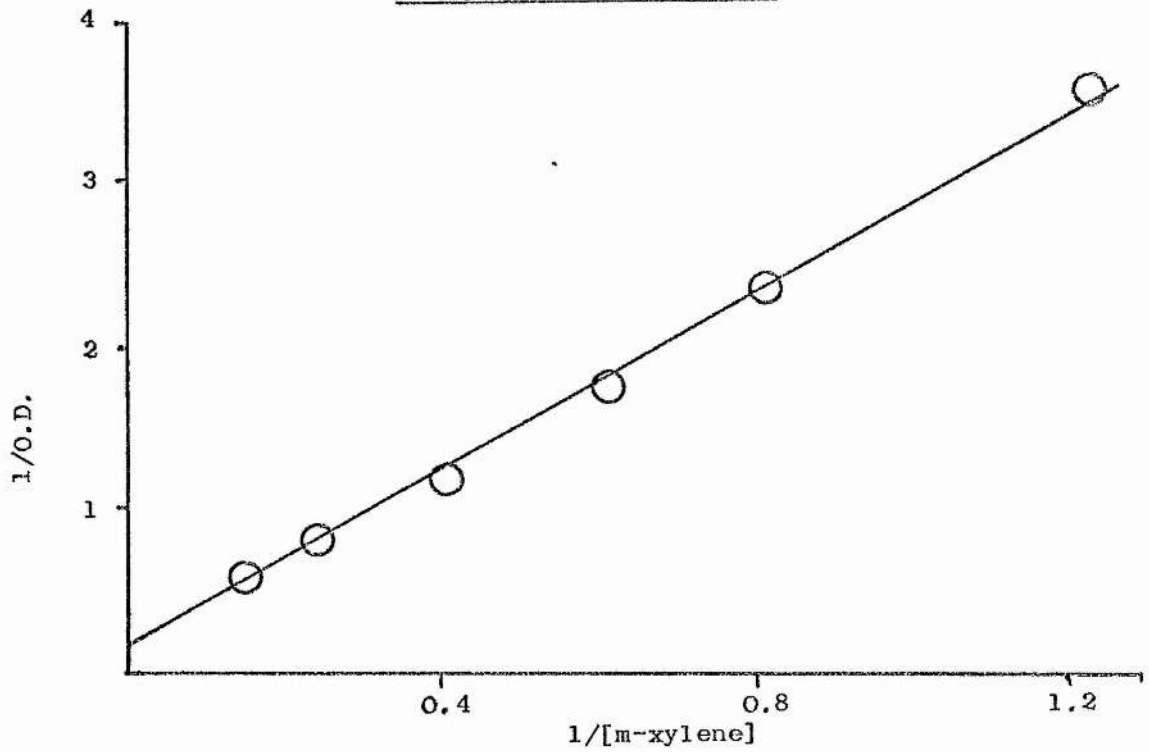
Determination of E and K for the iodine-m-xylene charge transfer complex at 25°.

[m-xylene]/M	O.D.[a]	$\frac{1}{[\text{m-xylene}]}$	$\frac{1}{\text{O.D.}}$
6.52	1.78	0.153	0.562
4.07	1.24	0.245	0.810
2.45	0.87	0.409	1.16
1.63	0.58	0.614	1.74
1.22	0.43	0.818	2.35
0.82	0.29	1.23	3.57

[a] at 320 nm and corrected for iodine absorption.

$[I_2] = 2.8 \times 10^{-3}$ M

Figure 25. Determination of E and K for the iodine-m-xylene charge transfer complex.



4. DETERMINATION OF THE VALUES OF H_o OF NITRIC ACID IN 10% AQUEOUS ACETIC ACID AT 25°.

This method is based on that described by Noyce and Castelfranco[169].

2-Nitroaniline and 4-nitroaniline were used as indicators. A solution of 2-nitroaniline (14.95 mg) in 10% aqueous acetic acid (50 ml) and a solution of 4-nitroaniline (7.33 mg) in 10% aqueous acetic acid (50 ml) were prepared. 4-Nitroaniline solution (1 ml) was added to each of solutions A-G, and 2-nitroaniline solution (1 ml) was added to each of solutions H-N, all these solutions being made up to 10 ml with the appropriate amounts of nitric acid and 10% aqueous acetic acid.

The optical densities of each of these solutions was measured in a 10 mm cell, in a thermostatted cell holder, by the use of a Unicam SP 500 spectrophotometer. Solutions A-G were measured at 383 nm and solutions H-N were measured at 412 nm.

Using the equation;

$$H_o = pK_a + \log[B]/[BH^+]$$

where [B] is the concentration of unprotonated indicator

$[BH^+]$ is the concentration of protonated indicator,

and pK_a is the pK_a of the indicator,

the values of the Hammett acidity function H_o were calculated for each concentration of nitric acid, Table 24, and plotted against the concentration of nitric acid, Figure 26.

TABLE 24

Determination of H_o for nitric acid in 10% aqueous acetic acid at 25°.

Solution	$[HNO_3]$/M	O.D.	H_o
A	0.0	1.28	-
B	0.019	0.90	1.36
C	0.039	0.70	1.07
D	0.077	0.49	0.79
E	0.154	0.3 5	0.56
F	0.222	0.23	0.32
G	0.309	0.19	0.22
H	0.0	1.04	-
I	0.193	0.94	0.45
J	0.386	0.83	0.06
K	0.772	0.67	-0.26
L	1.178	0.51	-0.54
M	1.544	0.38	-0.75
N	1.737	0.34	-0.84

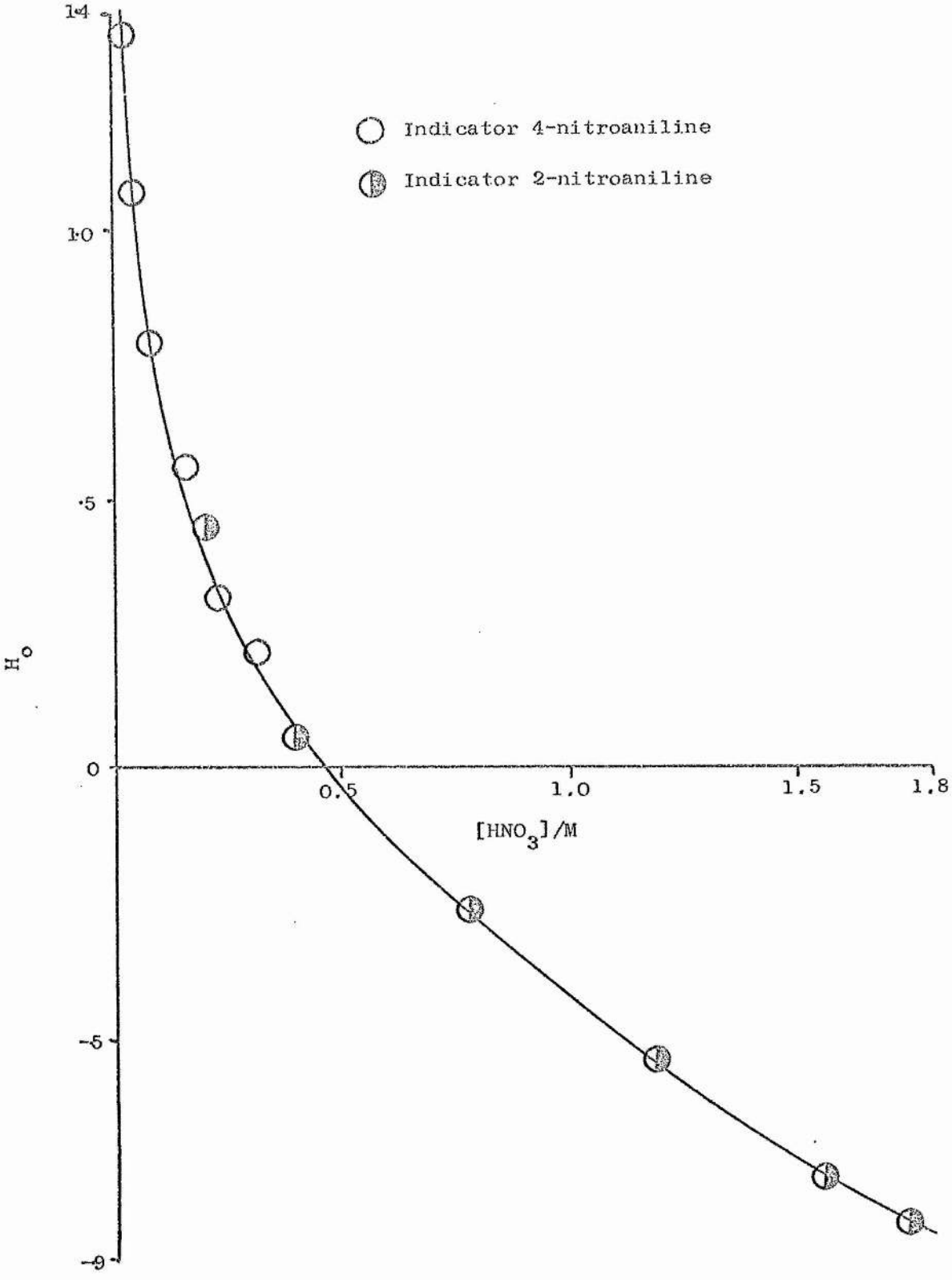
pK_a for 2-nitroaniline = -0.52

pK_a for 4-nitroaniline = -0.99

The optical densities of the fully protonated indicators at the respective wavelenghts was found to be 0.0 in both cases.

Figure 26

Figure 26. Acidity function data for nitric acid in 10% acetic acid.



5. DETERMINATION OF THE MOLAR EXTINCTION COEFFICIENTS OF IODINE IN ACETIC ACID AND TRIFLUOROACETIC ACID/ACETIC ACID AT 25°C.

The spectrum of iodine (1.29×10^{-3} M) in acetic acid was drawn on a Unicam SP800 spectrophotometer using 10 mm cells in a thermostatted cell holder. The curve showed as maximum due to iodine, or more probably to a complex of iodine and acetic acic[122] at 475nm. Several solutions of iodine at different concentrations were prepared in acetic acid and the optical densities of these solutions were measured at 475 nm by the use of a Unicam SP500 spectrophotometer, Table 25. A graph of the concentration of iodine against the corresponding optical density was plotted, Figure 27. By Beers' Law;

Optical density = E x d x concentration of species

where E is the molar extinction coefficient and d is the path length.

Therefore the gradient of the graph in Figure 27 is the molar extinction coefficient.

Gradient = 768.7

$\therefore$ E = 769

An analogous proceedure was followed for iodine in a 1:1 mixture of acetic acid and trifluoroacetic acid, the maximum absorption occurring at 500 nm. The results from this experiment are displayed in Table 26 and Figure 28.

Gradient = 844.9

$\therefore$ E = 845

TABLE 25

Determination of E for iodine in acetic acid at 25°

10^4[Iodine]/M	O.D. at 475 nm
2.59	0.20
5.19	0.39
7.80	0.60
10.4	0.80
12.9	0.99

Figure 27

TABLE 26

Determination of E for iodine in 1:1 acetic acid, trifluoroacetic acid at 25°

10^4[Iodine]/M	O.D. at 500 nm
2.59	0.23
5.19	0.43
7.81	0.66
10.4	0.88
13.0	1.10

Figure 28

Figure 27. Extinction coefficient of iodine in acetic acid.

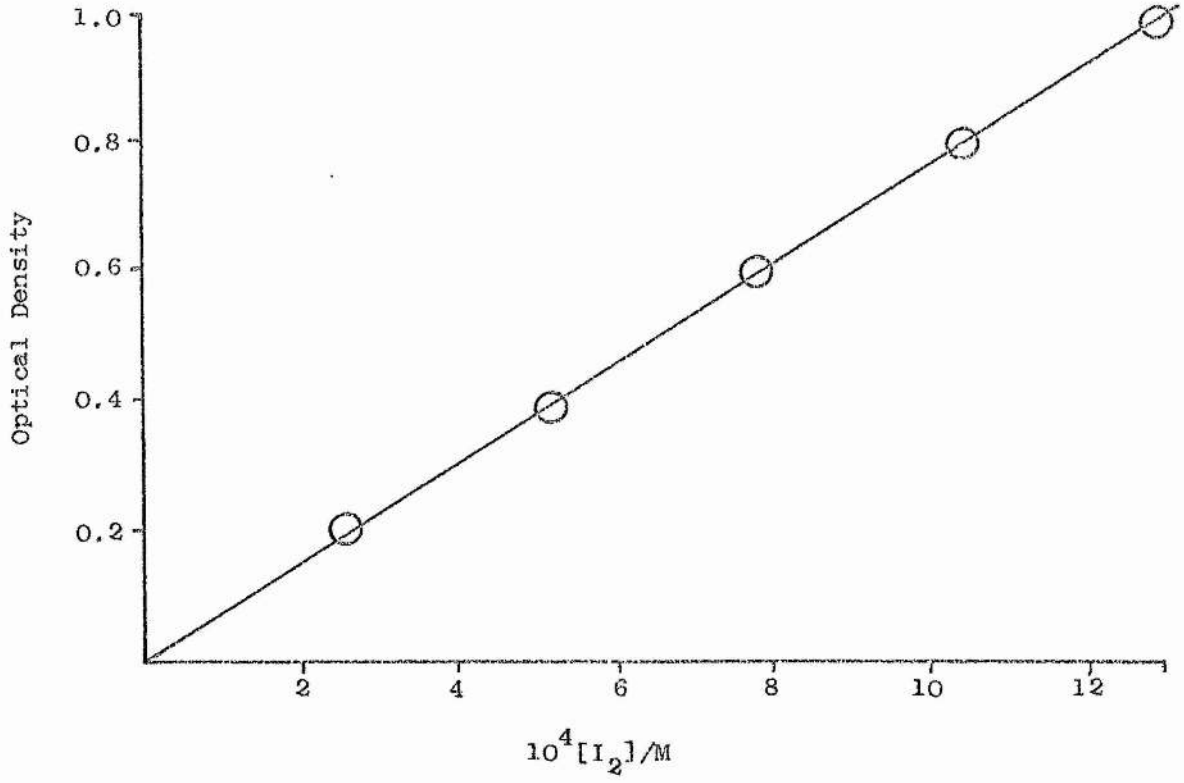
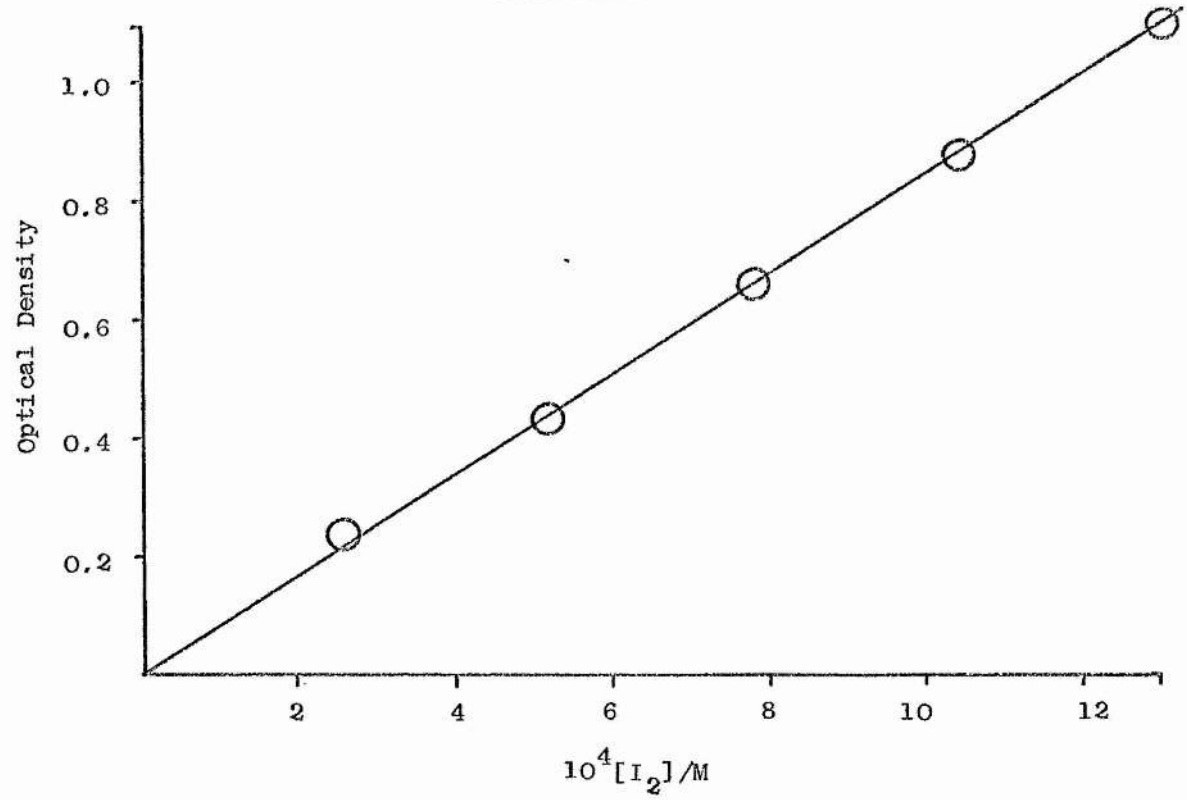


Figure 28. Extinction coefficient of iodine in acetic acid/ trifluoroacetic acid.



6. INVESTIGATION OF THE EFFECT OF LITHIUM SALTS ON THE RATE OF NITRODEIODINATION OF 2,4-DI-IODOANISOLE AT 25°.

Various lithium salts, which are soluble in acetic acid, were added to solutions of 2,4-di-iodoanisole (0.008 g) and sodium nitrite (0.035 g) in acetic acid (5 ml) and nitric acid (5 ml). The spectra of each of these solutions, in a 1 cm cell in a thermostatted cell holder, were drawn by the use of a Unicam SP 800 spectrophotometer, at definite time intervals until the reaction was complete.

Lithium bromide and iodide were found to decompose to give bromine and iodine, respectively, when added to the acetic acid, nitric acid mixture and so could not be used. Lithium chloride and lithium fluoride were found to complex with free molecular iodine and it was these complexes that were monitored. The reaction proceeded normally in the presence of lithium nitrate and lithium perchlorate.

The reaction in the presence and absence of these lithium salts was found to be first order with respect to released iodine (or complex), and half-lives in all cases were found to be identical within experimental error in all cases. In the cases where complexes formed there was an induction period before the first order reaction commenced and it was the half-life of this latter part of the reaction that was calculated. The complexes were assumed to be I_2Cl^- and I_2F^- which have been previously reported[170]. The results of this experiment are displayed in Table 27.

TABLE 27

The effect of lithium salts on the nitrodeiodination of 2,4-di-iodoanisole at 25°

Lithium salt added	10^{-2} (half-life of reaction)/s
None	1.58
$LiNO_3$	1.54
$LiClO_4$	1.56
LiCl	1.64
LiF	1.62

7. IODINATION OF SUBSTITUTED BENZENES AND THIOPHENS

Kinetic procedure

A solution of iodine in acetic acid (ca. 0.001 M) at 25° was added to a weighed quantitiy of the substrate and a measured volume of sodium nitrite solution (0.05 M) in a 10 ml volumetric flask. The reaction was started by the addition of nitric acid, and a 10 mm spectrophotometer cell was filled with this mixture and placed in the thermostatted cell holder of a Unicam SP 500 spectrophotometer. The disappearance of absorbance at 475 nm was then monitored for longer than three half-lives and a residual optical density was measured after about six half-lives.

The substrate, sodium nitrite and nitric acid were present in large excess over iodine, giving pseudo half-order reaction kinetics, and the rate constants, k(obs.), were calculated from plots of the square-root of $(D_t - D_\infty)$ against time, where D_t and D_∞ represent the optical densities after time, t, and at infinite time respectively. Such plots were rectilinear over at least three half lives. The value of $(D_t - D_\infty)$ is proportional to the concentration of iodine at time, t, with the constant of proportionality being the reciprocal of the molar extinction coefficient of iodine:

$$[I_2]_t = \frac{(D_t - D_\infty)}{E}$$

For the integration of the half order rate equation see Appendix 3.

The variation, with time, of the full spectrum, between 450-800 nm, of the iodination of all the substrates, was recorded by use of Unicam SP800 spectrophotometer. These spectra all showed tight isosbestic points, the significance of which has been discussed[171,172,173].

Results obtained in the later experiments were analysed by the use of computer programme APKINE, (see Appendix 5).

TABLE

Iodination of m-xylene in 10% aqueous acetic acid with a trace of sodium nitrite present at 25°.

Specimen Experiment 1

$[I_2]_o = 1.29 \times 10^{-3}$ M $[HNO_3] = 1.56$ M

$[NaNO_2]$ - trace [m-Xylene] = 0.99 M

Wavelength 475 nm

Time/s	$(D_t - D_\infty)$
0.0	0.795
85.7	0.770
171.4	0.724
257.1	0.648
342.8	0.568
428.5	0.469
514.2	0.351
599.9	0.256
685.6	0.155
771.3	0.058
857.0	0.010
942.7	0.001

Figure 29

The sigmoid nature of this curve is characteristic of an autocatalytic reaction. With sodium nitrite concentrations greater than 0.005 M the sigmoid nature disappears.

Iodination of m-xylene in 10% aqueous acetic acid at 25°

Specimen Experiment 2

$[I_2]_o = 1.24 \times 10^{-3}$ M $[HNO_3] = 1.56$ M

$[NaNO_2] = 5.0 \times 10^{-3}$ M [x-Xylene] = 0.339 M

Wavelength 475 nm

Time/s	$(D_t - D_\infty)$	$(D_t - D_\infty)^{\frac{1}{2}}$
0.0	0.588	0.767
21.4	0.506	0.711
42.8	0.426	0.652
64.3	0.358	0.598
85.7	0.287	0.536
107.1	0.226	0.475
128.6	0.171	0.414
150.0	0.121	0.348
171.4	0.090	0.300
192.8	0.061	0.247
214.3	0.037	0.192
236.8	0.020	0.141
257.1	0.007	0.084

Figure 30

$k(obs.) = 1.96 \times 10^{-4}$ mol$^{\frac{1}{2}}$ l$^{-\frac{1}{2}}$ s^{-1}

Figure 29. Iodination of m-xylene with a trace of nitrite present.

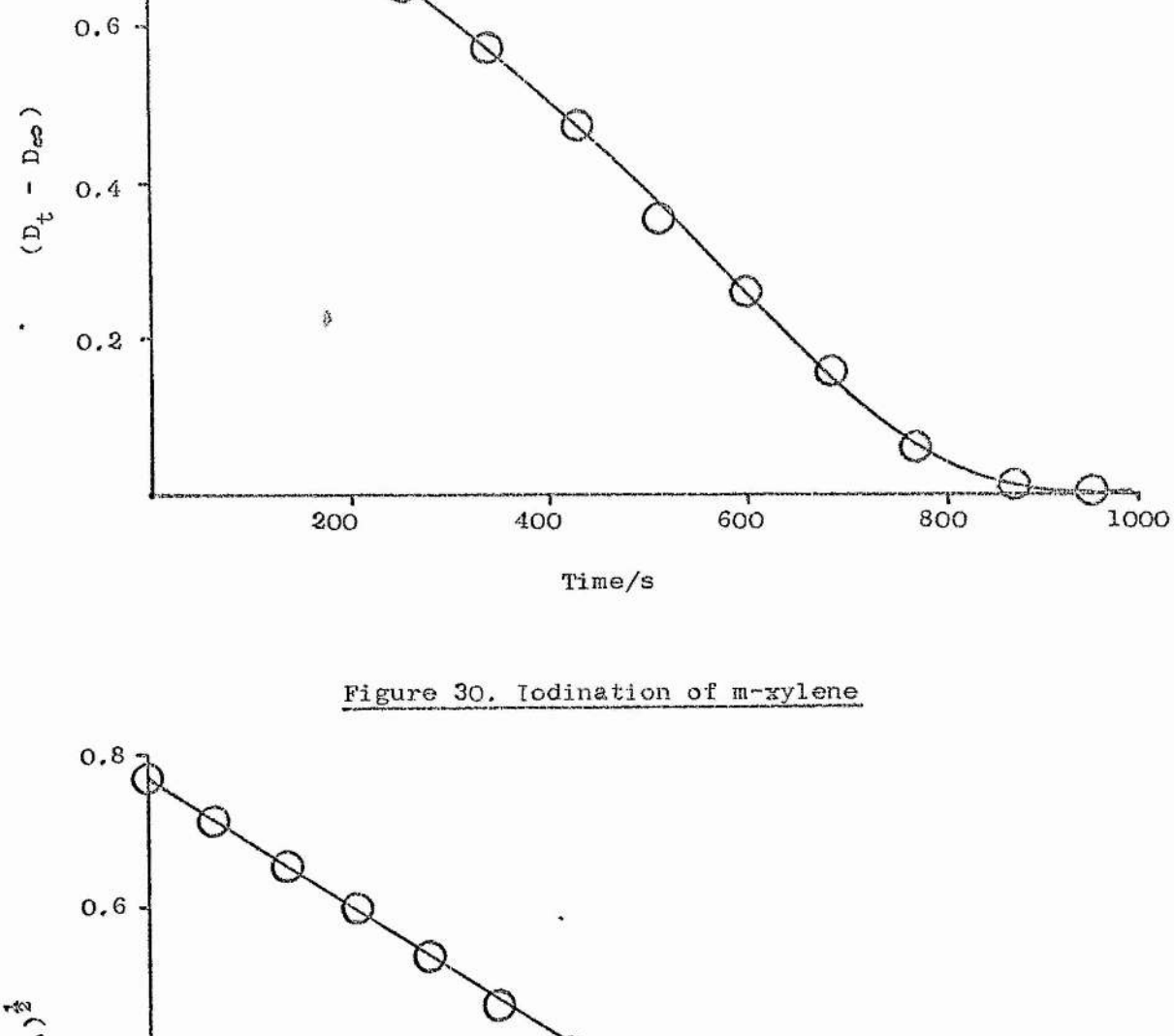
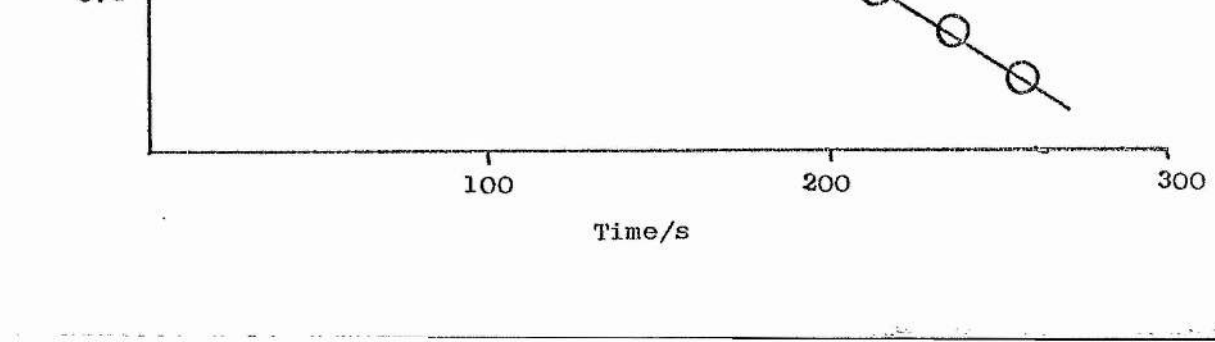


Figure 30. Iodination of m-xylene



Iodination of mesitylene in 10% aqueous acetic acid at 25°

Specimen Experiment 3

$[I_2]_o = 1.26 \times 10^{-3}$ M $[HNO_3] = 1.56$ M

$[NaNO_2] = 5.0 \times 10^{-3}$ M [Mesitylene] $= 1.68 \times 10^{-2}$ M

Wavelength 475 nm

Time/s	$(D_t - D_\infty)$	$(D_t - D_\infty)^{\frac{1}{2}}$
0.0	0.447	0.699
21.4	0.295	0.543
42.8	0.117	0.421
64.3	0.092	0.303
85.7	0.036	0.190
107.1	0.010	0.100
128.6	0.001	0.036

Figure 31

$k(obs.) = 4.07 \times 10^{-4}$ mol$^{\frac{1}{2}}$ l$^{-\frac{1}{2}}$ s^{-1}

Iodination of 2-bromo-anisole in 10% aqueous acetic acid at 25°.

Specimen Experiment 4

$[I_2]_o = 1.21 \times 10^{-3}$ M $[HNO_3] = 1.61$ M

$[NaNO_2] = 5.0 \times 10^{-3}$ M [2-Bromoanisole] = 0.204 M

Wavelength 475 nm

Time/s	$(D_t - D_\infty)$	$(D_t - D_\infty)^{\frac{1}{2}}$
0.0	0.621	0.788
85.7	0.482	0.694
171.4	0.361	0.601
257.1	0.253	0.503
342.8	0.170	0.412
428.5	0.096	0.310
514.2	0.045	0.212
599.9	0.015	0.123
685.6	0.002	0.045

Figure 32

$k(obs.) = 8.0 \times 10^{-3}$ $mol^{\frac{1}{2}}$ $l^{-\frac{1}{2}}$ s^{-1}

Figure 31. Iodination of mesitylene.

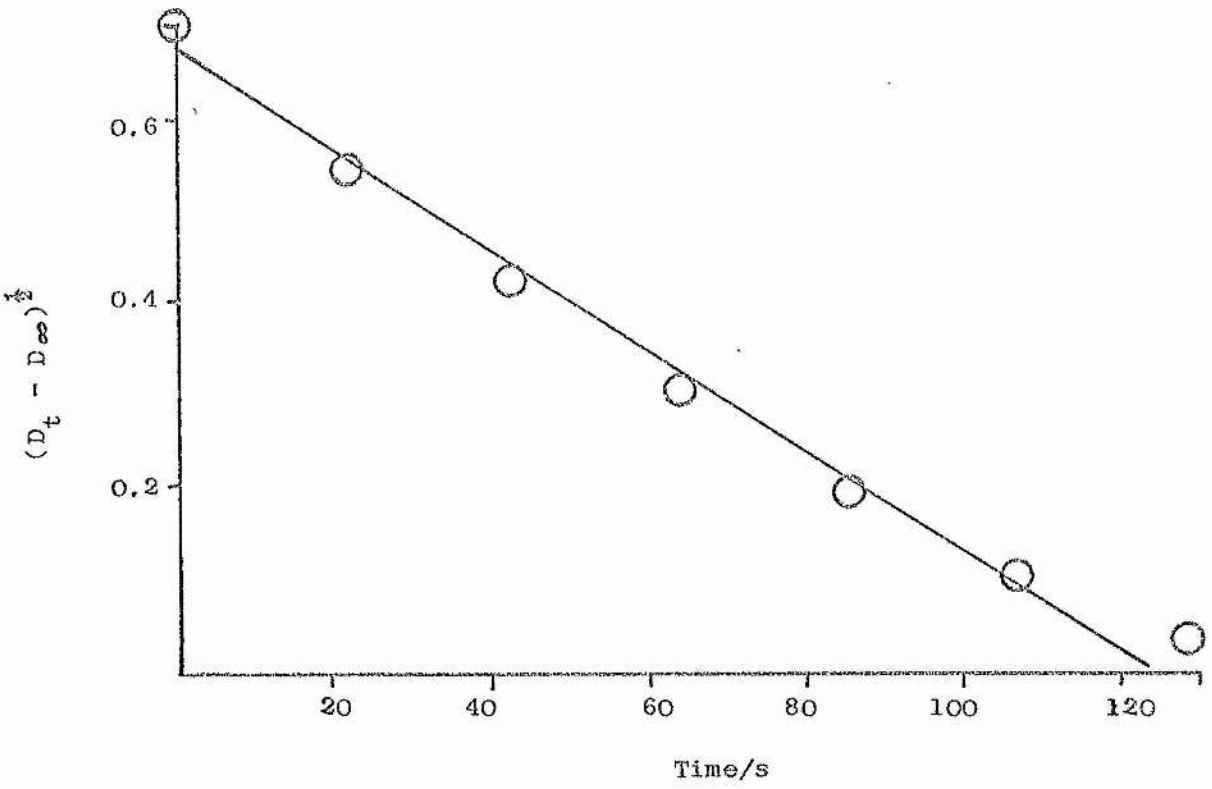
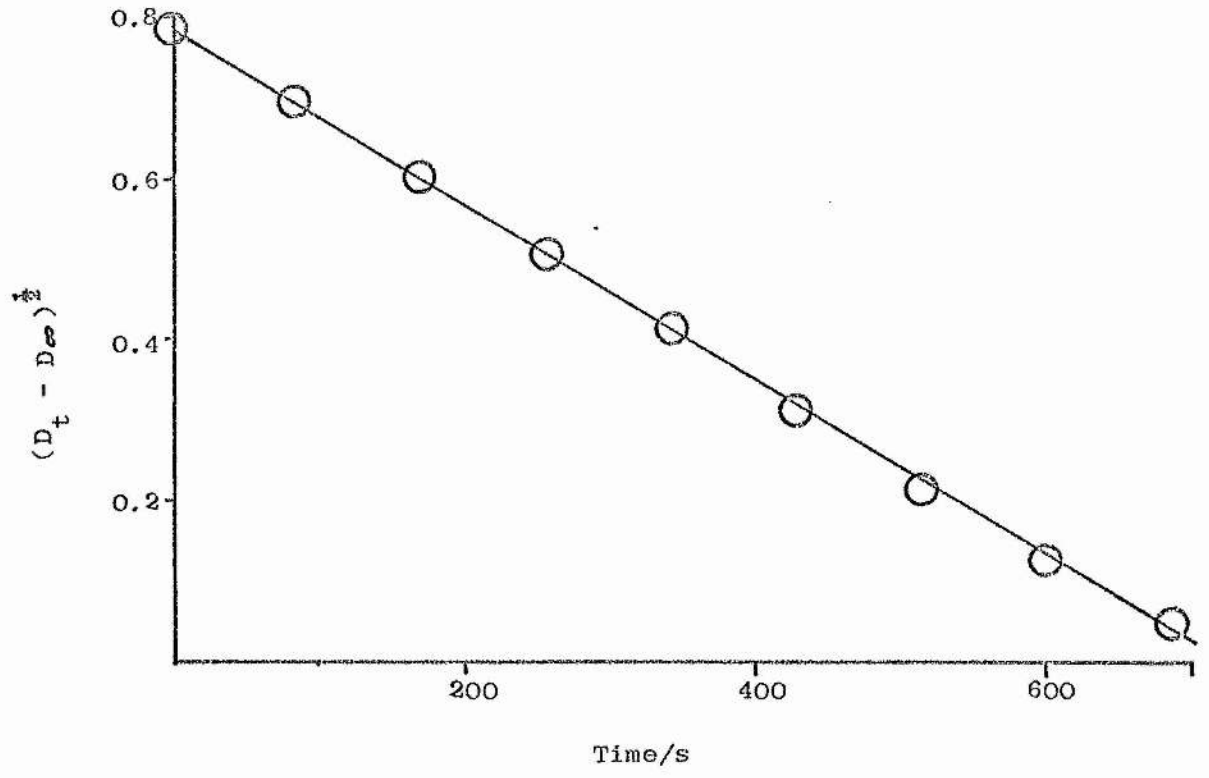


Figure 32. Iodination of 2-bromoanisole.



Iodination of toluene in a 50/50 mixture of acetic acid and trifluoroacetic acid containing 10% water at 25°.

Specimen Experiment 5

$[I_2]_o = 1.08 \times 10^{-3}$ M $[HNO_3] = 1.61$ M

$[NaNO_2] = 5.0 \times 10^{-3}$ M [Toluene] $= 4.98 \times 10^{-2}$ M

Wavelength 500 nm

Time/s	$(D_t - D_\infty)$	$(D_t - D_\infty)^{\frac{1}{2}}$
0.0	0.450	0.671
21.4	0.381	0.617
42.8	0.323	0.568
64.3	0.262	0.512
85.7	0.215	0.464
107.1	0.165	0.406
128.6	0.124	0.352
150.0	0.088	0.297
171.4	0.060	0.245
192.8	0.035	0.187
214.2	0.016	0.127
236.7	0.006	0.077

Figure 33

$k(obs.) = 1.74 \times 10^{-4}$ mol$^{\frac{1}{2}}$ l$^{-\frac{1}{2}}$ s^{-1}

Iodination of thiopen in 10% aqueous acetic acid at 25°

Specimen Experiment 6

$[I_2]_o = 1.24 \times 10^{-3}$ M $[HNO_3] = 0.161$ M

$[NaNO_2] = 5.0 \times 10^{-3}$ M [Thiophen] = 0.249 M

Wavelength 475 nm

Time/s	$(OD_t - OD_\infty)$	$(OD_t - OD_\infty)^{\frac{1}{2}}$
0.0	0.748	0.865
30.0	0.545	0.738
60.0	0.428	0.654
90.0	0.300	0.548
120.0	0.197	0.444
150.0	0.117	0.342
180.0	0.065	0.255
210.0	0.034	0.184
240.0	0.016	0.127

Figure 34

$k(obs.) = 2.67 \times 10^{-4}$ $mol^{\frac{1}{2}}$ $l^{-\frac{1}{2}}$ s^{-1}

Figure 33. Iodination of toluene.

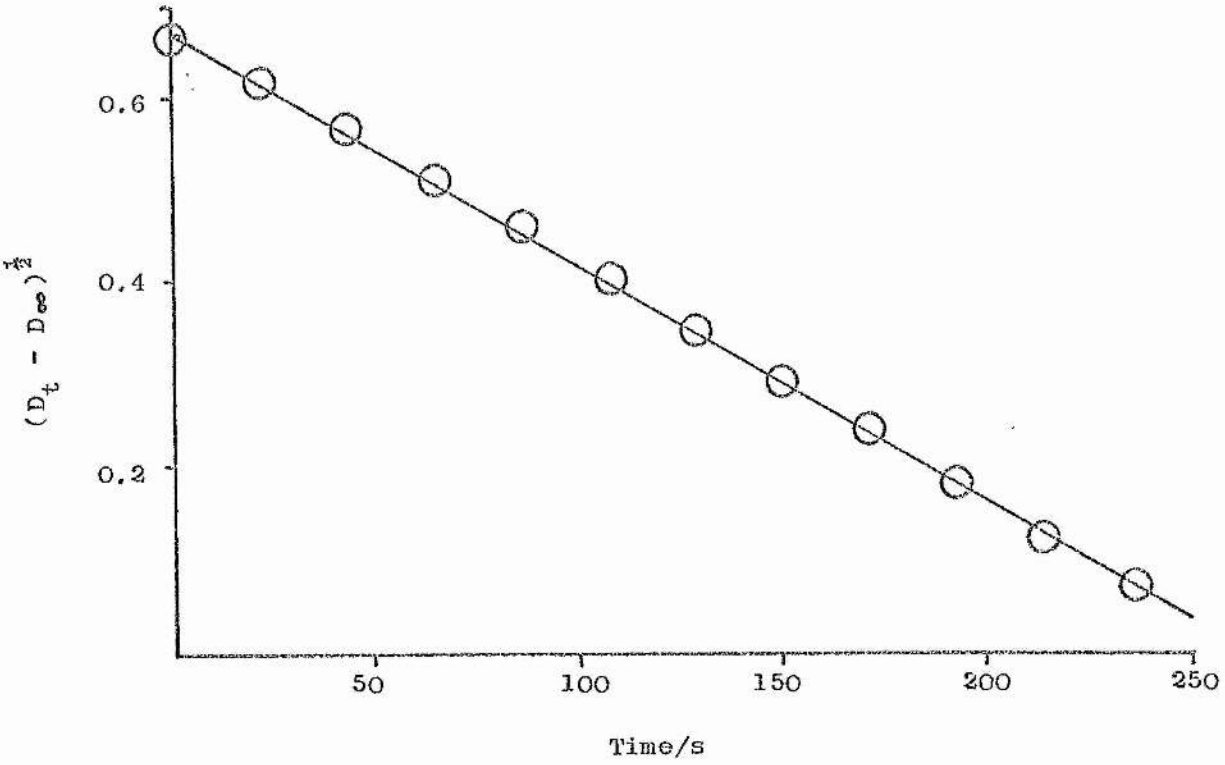
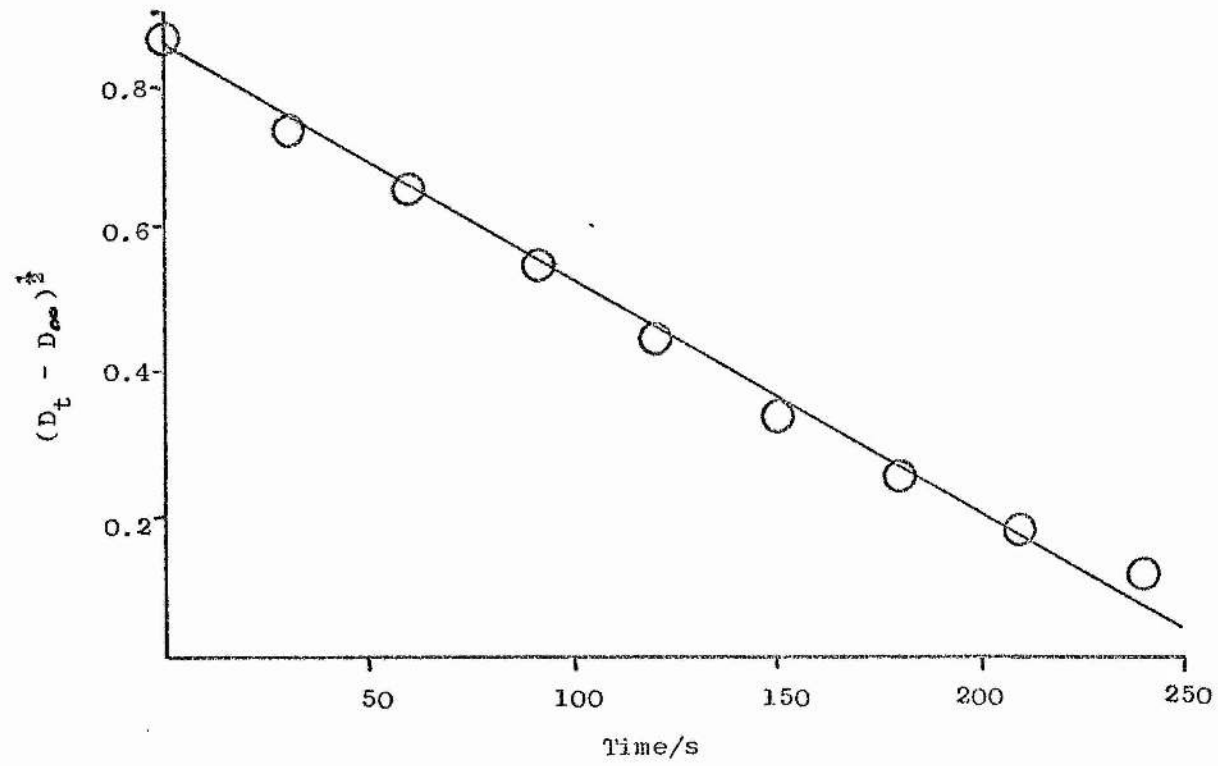


Figure 34. Iodination of thiophen.



Iodination of 2-chlorothiophen in 10% aqueous acetic acid at 25°

Specimen Experiment 7

$[I_2]_o = 1.24 \times 10^{-3}$ M $[HNO_3] = 0.161$ M

$[NaNO_2] = 5.0 \times 10^{-3}$ M [2-Chlorothiophen] = 0.488 M

Wavelength 475 nm

Time/s	$(D_t - D_\infty)$	$(D_t - D_\infty)^{\frac{1}{2}}$
0.0	0.939	0.966
60.0	0.762	0.873
120.0	0.601	0.775
180.0	0.454	0.674
240.0	0.320	0.566
300.0	0.207	0.455
360.0	0.113	0.336
420.0	0.054	0.232
480.0	0.018	0.134

Figure 35

$k(obs.) = 1.28 \times 10^{-4}$ $mol^{\frac{1}{2}}$ $l^{-\frac{1}{2}}$ s^{-1}

Iodination of 2-phenylthiophen in 10% aqueous acetic acid at 25°.

Specimen Experiment 8

$[I_2]_o = 1.23 \times 10^{-3}$ M $[HNO_3] = 0.161$ M

$[NaNO_2] = 5 \times 10^{-3}$ M [2-Phenylthiophen] = 6.76×10^{-2} M

Wavelength 475 nm

Time/s	$(D_t - D_\infty)$	$(D_t - D_\infty)^{\frac{1}{2}}$
0.0	0.634	0.796
60.0	0.450	0.671
120.0	0.316	0.562
180.0	0.206	0.454
240.0	0.124	0.352
300.0	0.067	0.259
360.0	0.034	0.184
420.0	0.015	0.123
480.0	0.002	0.045

Figure 36

$k(obs.) = 1.08 \times 10^{-3}$ $mol^{\frac{1}{2}}$ $l^{-\frac{1}{2}}$ s^{-1}.

Figure 35. Iodination of 2-chlorothiophen.

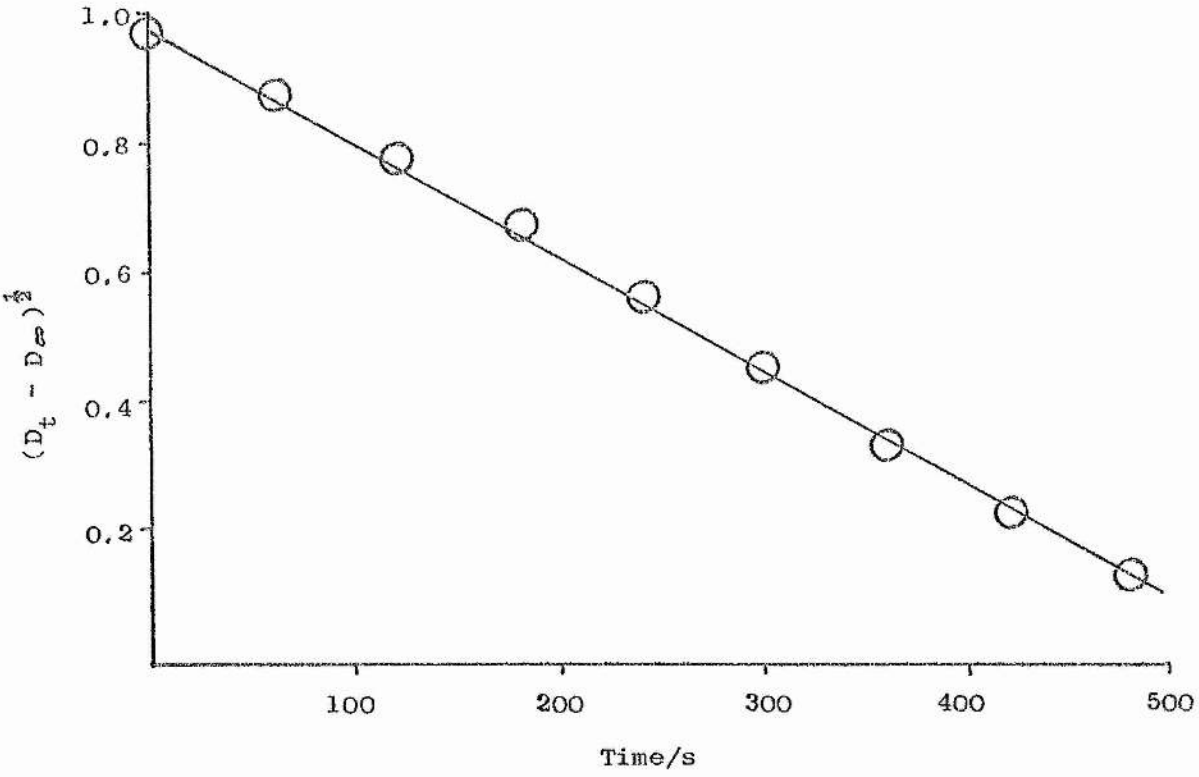
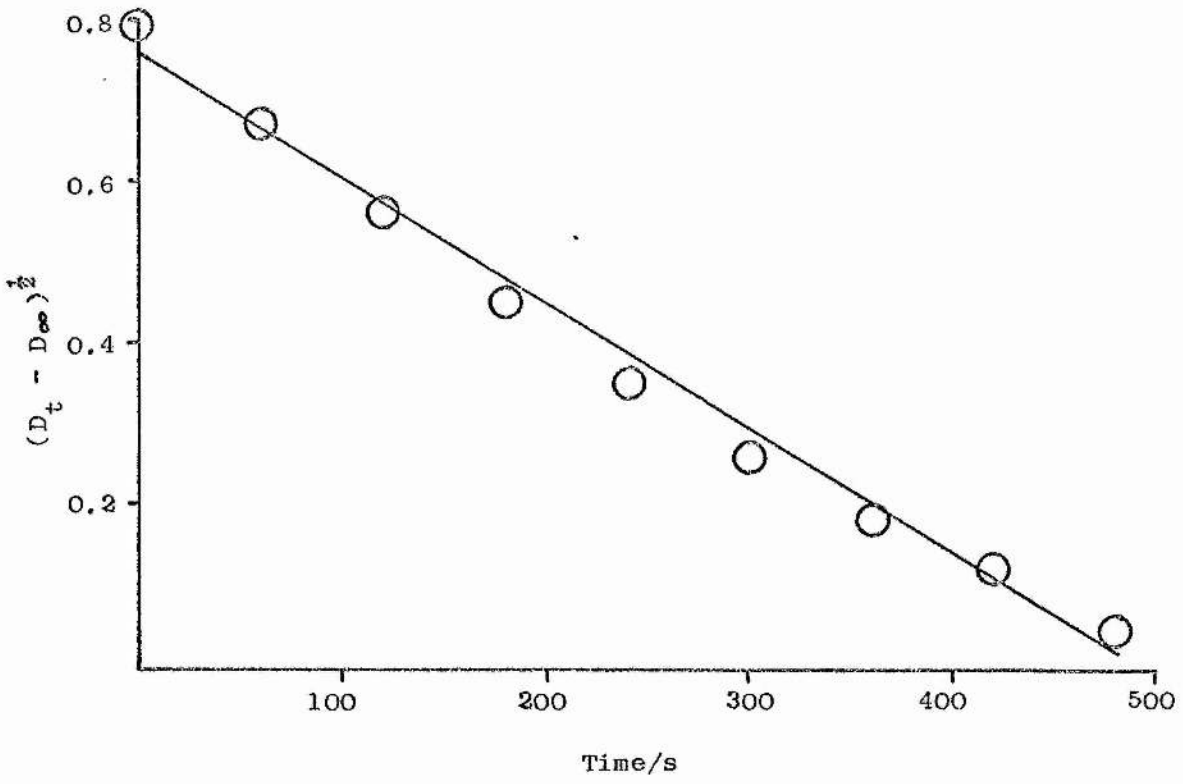


Figure 36. Iodination of 2-phenylthiophen.



8. NITRODEIODINATION OF ACTIVATED AROMATIC IODOCOMPOUNDS

Kinetic procedure

A weighed quantity of substrate was dissolved in acetic acid, at 25°, in a 10 ml volumetric flask. The reaction was started by the addition of a solution of sodium nitrite in nitric acid, and a 10 mm spectrophotometer cell was filled with this mixture and placed in the thermostatted cell holder of a Unicam SP500 or a Unicam SP700 spectrophotometer. The disappearance of absorption at a chosen wavelength (usually 475 nm) was then monitored for longer than three half-lives and a residual optical density was measured after about ten half-lives.

The nitric acid and sodium nitrite were present in large excess over the substrate, giving pseudo first-order reaction conditions, and the observed rate constants, k(obs.), were calculated from plots of $\log_{10}(D_\infty - D_t)$ against time, where D_t and D_∞ represent the optical densities at time, t, and infinite time respectively. Such plots were rectilinear over at least three half-lives.

The variation, with time, of the full spectrum, between 450-800 nm, of the reaction of all substrates, was recorded by the use of a Unicam SP800 spectrophotometer.

The results obtained in the later experiments were analysed by the use of computer programme APKINE (see Appendix 5).

The reaction of 4-iodoanisole in acetic acid with nitric acid and sodium nitrite was also studied by the use of a Canterbury Stopped Flow apparatus, the spectra being recorded on Polaroid film from an Advance OS3000 oscilloscope.

Nitrodeiodination of 4-iodoanisole in acetic acid at 25°

Specimen Experiment 9

$[HNO_3]$ = 8.05 M $[NaNO_2]$ = 0.025 M

$[4\text{-Iodoanisole}]_o = 5.31 \times 10^{-3}$ M

Wavelength 475 nm

Time/s	$(D_\infty - D_t)$	$3 + \log (D_\infty - D_t)$
0.0	0.611	2.786
84.0	0.421	2.624
204.0	0.254	2.405
324.0	0.157	2.196
444.0	0.092	1.964
564.0	0.058	1.763
684.0	0.037	1.568
804.0	0.021	1.322
924.0	0.010	1.000
1044.0	0.006	0.778

Figure 37

$k(obs.) = 4.14 \times 10^{-3}\ s^{-1}$

Nitrodeiodination of 2,4-iodoanisole in acetic acid at 25°.

Specimen Experiment 10

$[HNO_3]$ = 8.05 M $[NaNO_2]$ = 0.025 M

$[2,4\text{-Di-iodoanisole}]_o = 2.65 \times 10^{-3}$ M

Wavelength 475 nm

Time/s	$(D_\infty - D_t)$	$3 + \log(D_\infty - D_t)$
0.0	0.620	2.792
132.0	0.334	2.524
252.0	0.196	2.292
372.0	0.113	2.053
492.0	0.072	1.857
612.0	0.040	1.602
732.0	0.024	1.380
852.0	0.012	1.079
972.0	0.008	0.903
1092.0	0.005	0.699

Figure 38

$k(obs.) = 4.19 \times 10^{-3}\ s^{-1}$

Figure 37. Nitrodeiodination of 4-iodoanisole.

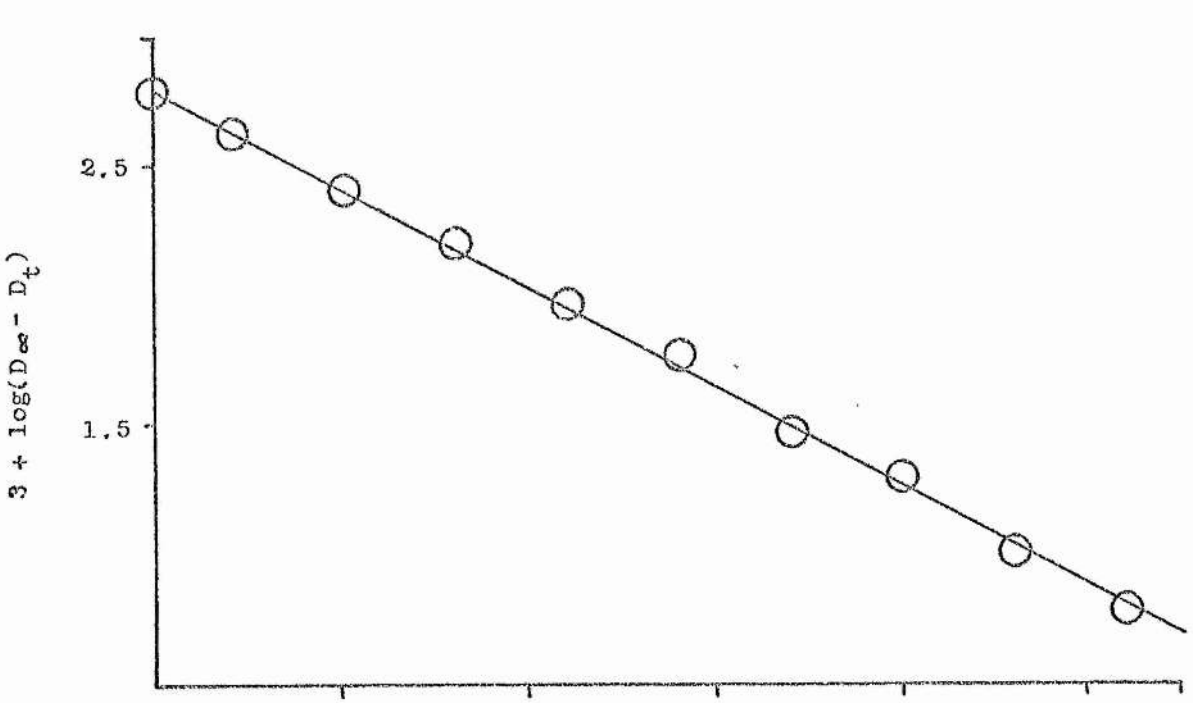
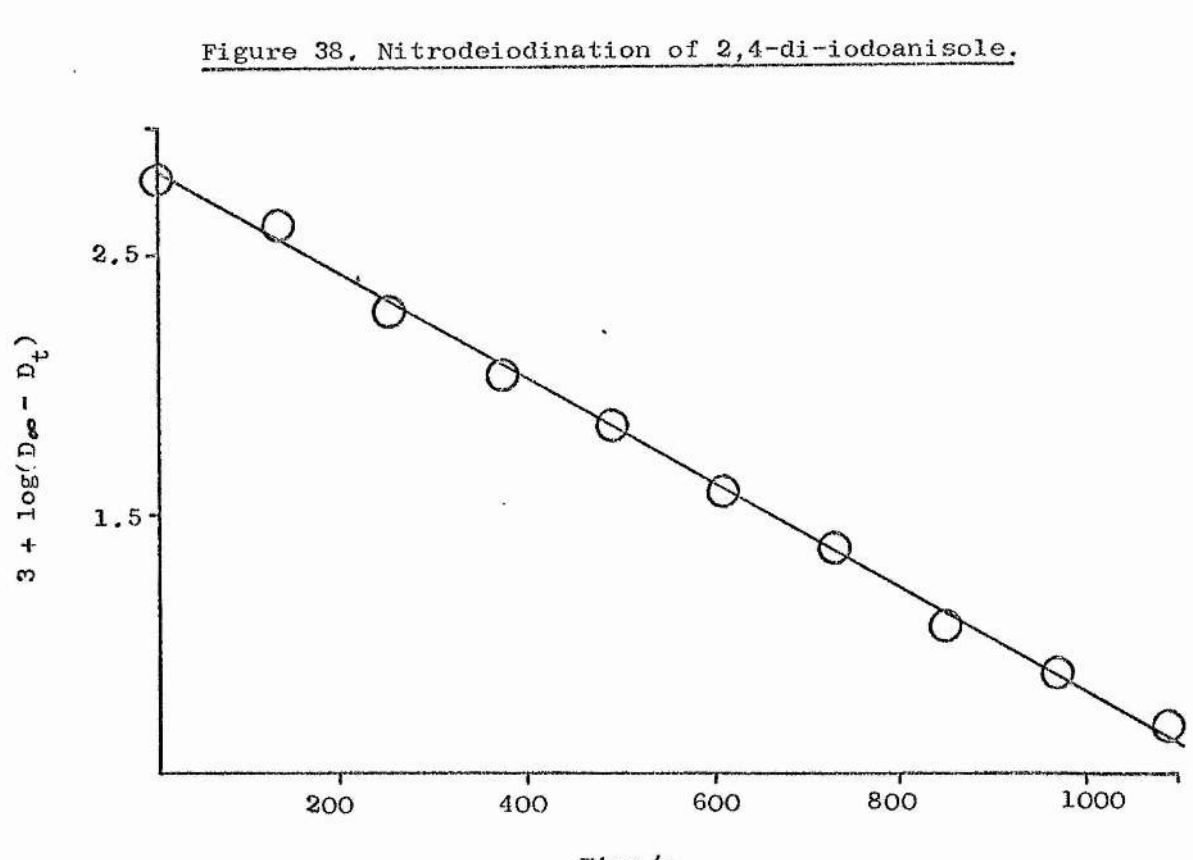


Figure 38. Nitrodeiodination of 2,4-di-iodoanisole.



Nitrodeiodination of 4-iodo-2,6-dimethylanisole in acetic acid at 25°

Specimen Experiment 11

$[HNO_3]$ = 4.83 M $[NaNO_2]$ = 0.041 M

$[4\text{-Iodo-2,6-dimethylanisole}]_o = 2.4 \times 10^{-3}$ M

Wavelength 475 nm

Time/s	$(D_\infty - D_t)$	$2 + \log (D_\infty - D_t)$
0.0	0.838	1.923
60.0	0.580	1.763
120.0	0.390	1.591
180.0	0.261	1.417
240.0	0.179	1.253
300.0	0.114	1.057
360.0	0.073	0.863
420.0	0.050	0.699
480.0	0.032	0.505
540.0	0.019	0.279

Figure 39

$k(obs.) = 7.05 \times 10^{-3}\ s^{-1}$

Nitrodeiodination of 4-iodophenol in acetic acid at 25°

Specimen Experiment 12

$[HNO_3]$ = 6.4 M $[NaNO_2]$ = 0.035 M

$[4\text{-Iodophenol}]_o = 3.6 \times 10^{-3}$ M

Wavelength 500 nm

Time/s	D_t
0	0.417
622	0.506
1244	0.593
2488	0.677
3732	0.724
4976	0.752
6220	0.775
7464	0.795
8708	0.811
11196	0.849
13684	0.883
16172	0.910

This reaction did not produce a first-order curve but is plotted in Figure 40.

Figure 39. Nitrodeiodination of 4-iodo-2,6-dimethylanisole.

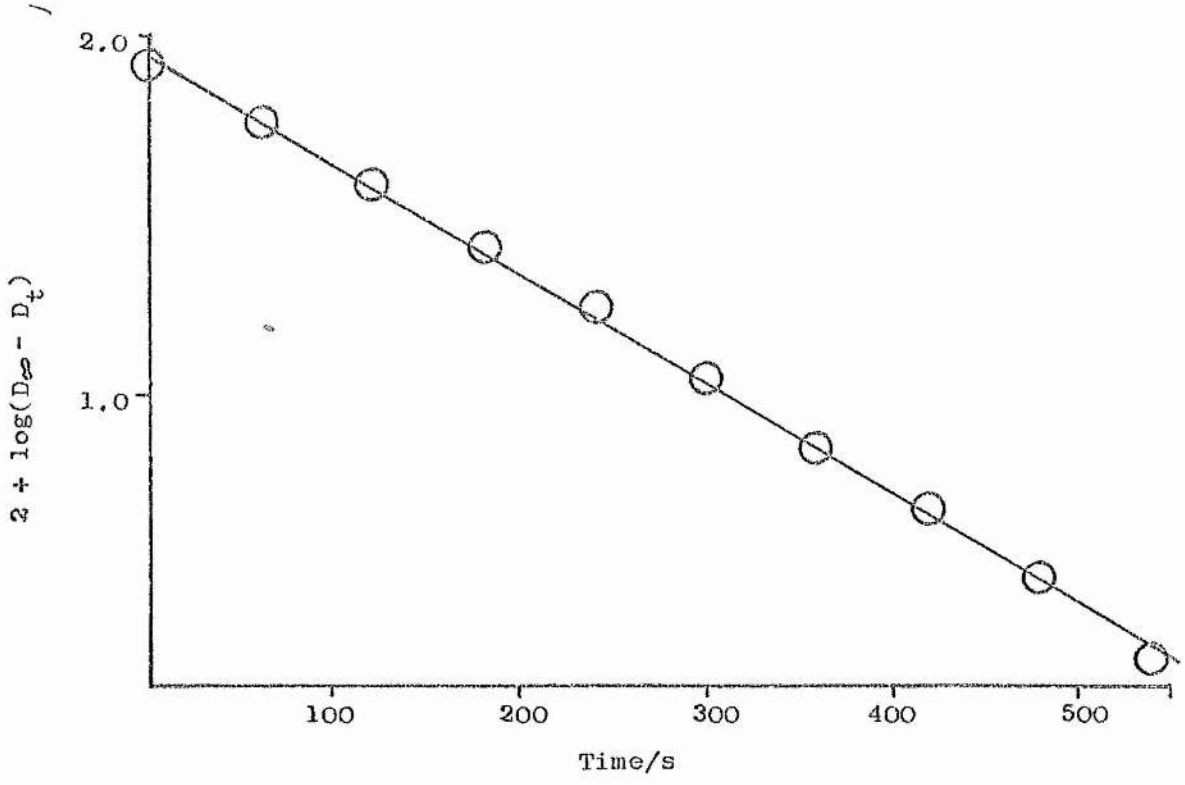
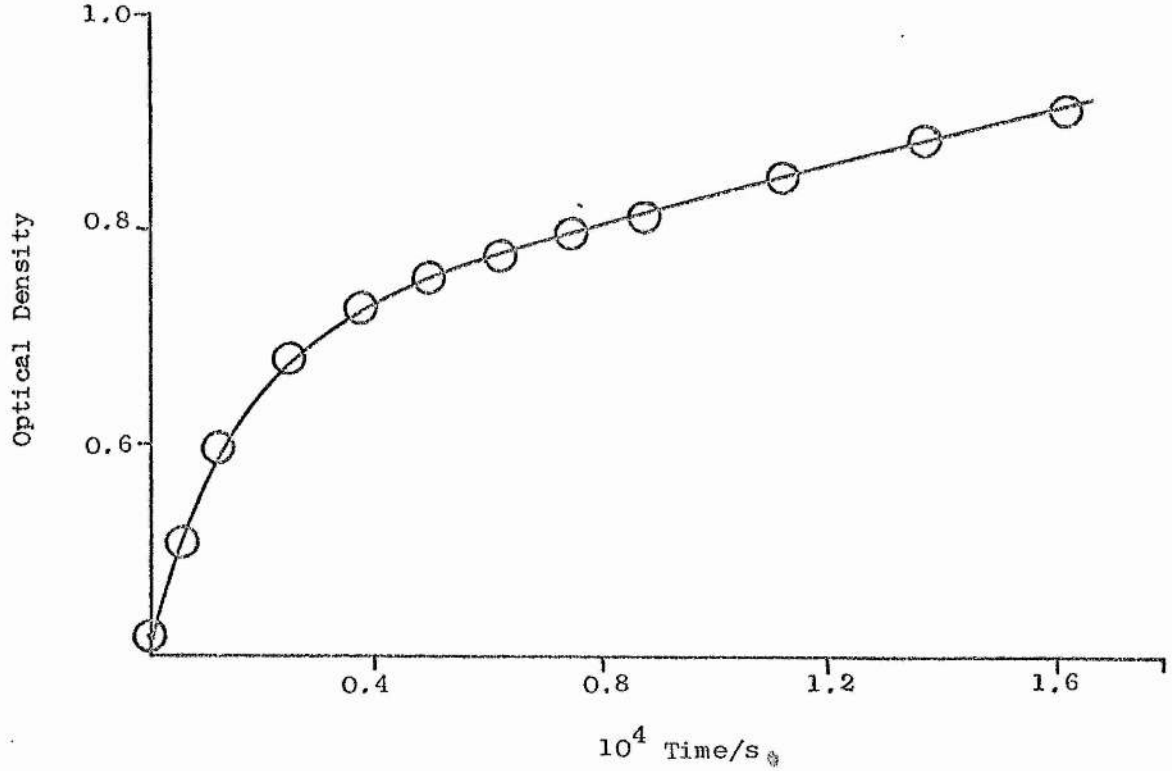


Figure 40. Nitrodeiodination of 4-iodophenol.



Nitrodeiodination of the sodium salt of 2-(4-iodophenoxy)-ethylsulphonic acid in water at 25°.

Specimen Experiment 13

$[HClO_4] = 7.2$ M $\qquad [NaNO_2] = 0.003$ M

$[\text{Sodium salt of 2-(4-iodophenoxy)-ethylsulphonic acid}]_o = 8.6 \times 10^{-5}$ M

This substrate was deiodinated by sodium nitrite and perchloric acid in water but an intense colouration interfered with the observation of the peak due to free iodine. The concentration of the substrate was decreased and the brown colour was monitored at 410 nm.

The change in optical density at 410 nm with time is shown in Figure 41.

Action of sodium nitrite and perchloric acid on the sodium salt of 2-phenoxy-ethylsulphonic acid in aqueous solution at 25°.

Specimen Experiment 14

$[HClO_4] = 7.2$ M $\qquad [NaNO_2] = 0.003$ M

$[\text{Sodium salt of 2-phenoxy-ethylsulphonic acid}]_o = 9.9 \times 10^{-5}$ M

The brown colour was monitored at 410 nm as in the above experiment and the change in optical density with time produced a curve of the same shape as that for the above experiment.

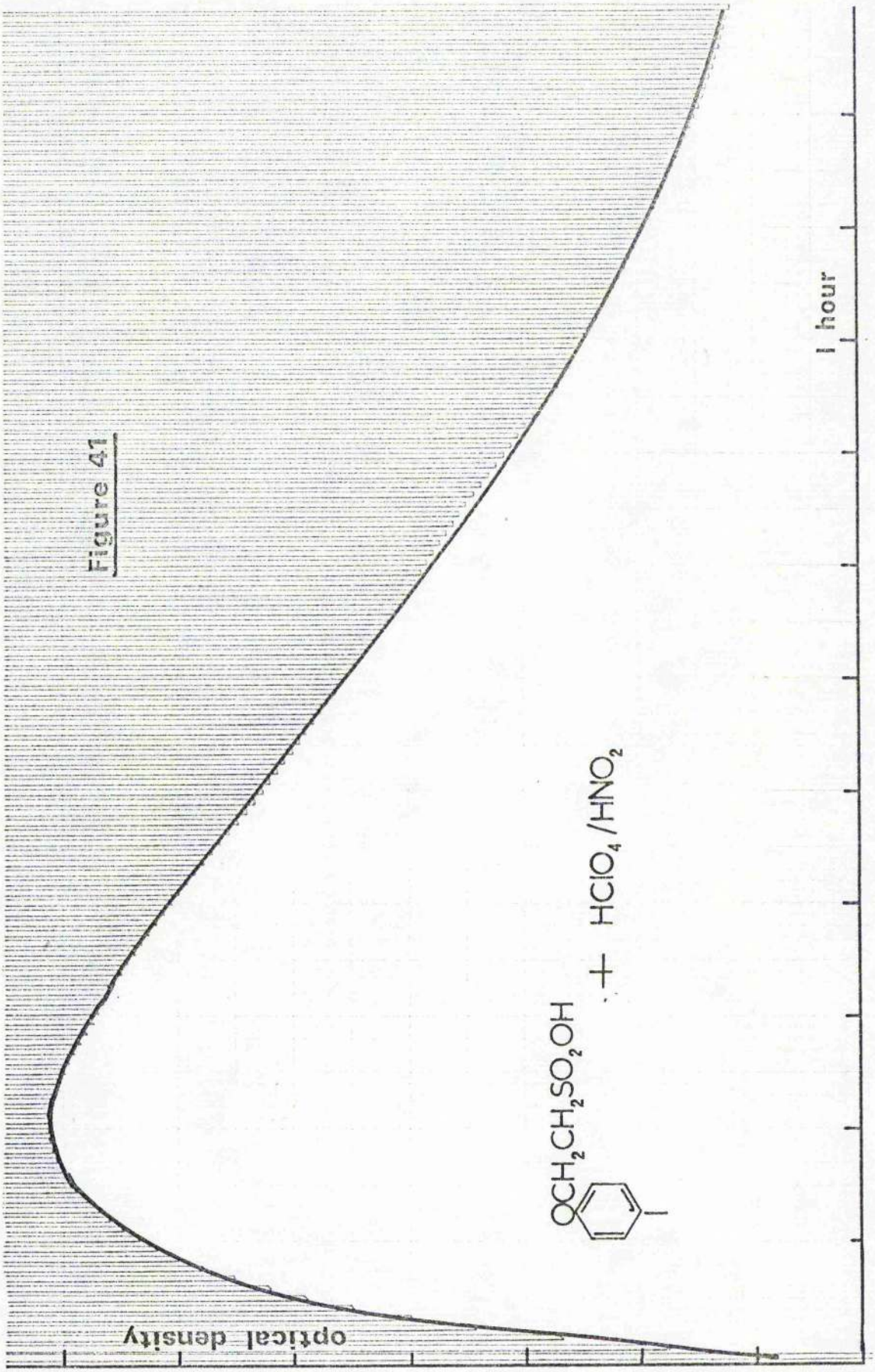


Figure 41

Study of the initial spectral changes during the nitrodeiodination of 4-iodoanisole at 25°.

When the nitrodeiodination of 4-iodoanisole is carried out, under the normal conditions, a yellow colouration is observed on mixing the reactants, but this colour disappears before the solution can be observed by a normal spectrophotometer. Therefore, it was decided to study this initial charge, only, by the use of stopped flow techniques.

A Canterbury SF apparatus was used, and in this apparatus stock solutions of the reactants were kept in reservoirs and thermostatted in glass coils before mixing in a thermostatted cell through which light was passed by means of light guides. The signal from a photomultiplier tube was fed to an Advance OS3000 oscilloscope, and a photograph, of the display was taken on Polaroid film. Examples of these photographs are given in Figures 42 and 43.

From these photographs the spectrum from 380-490nm of the yellow colour after 10s was built up.

Figure 42. First minute of nitrodeiodination of 4-iodoanisole at 420nm.

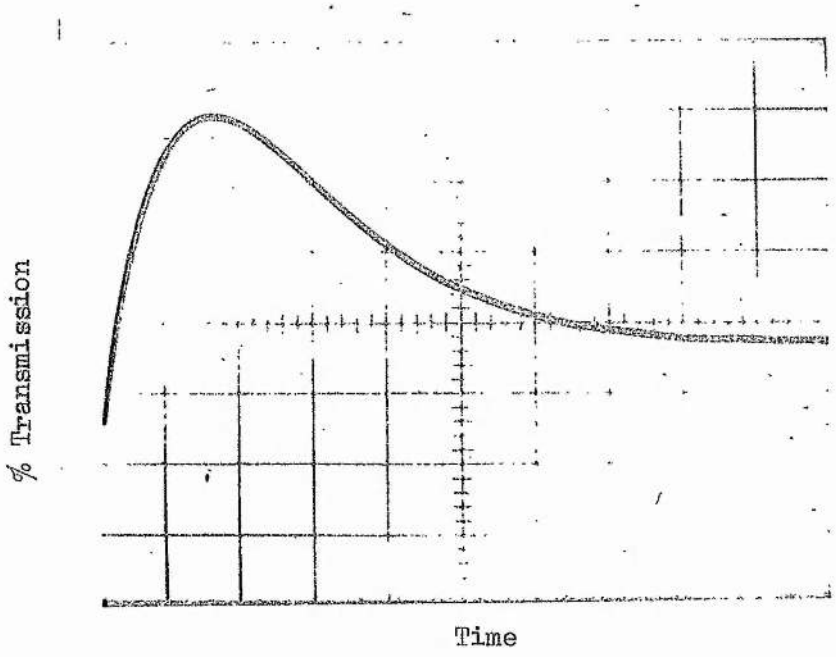
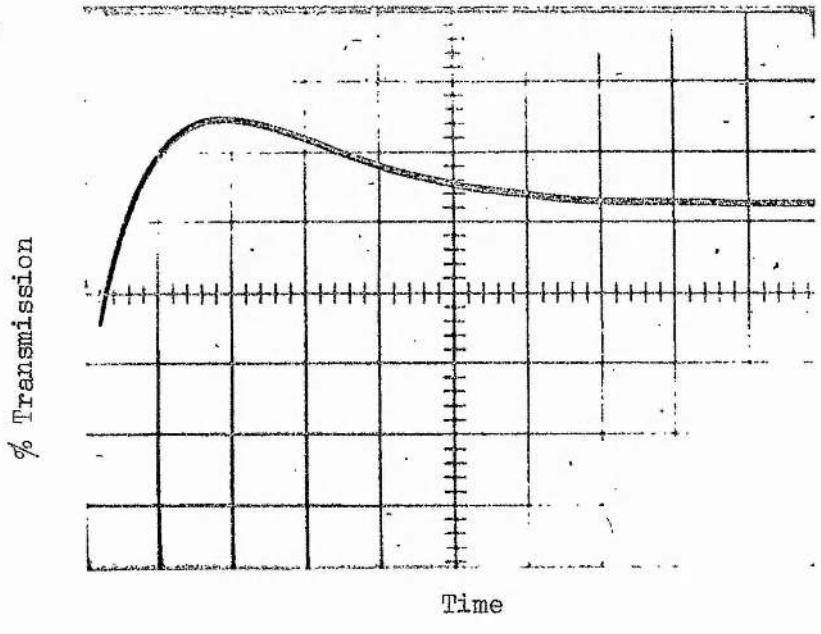


Figure 43. First minute of nitrodeiodination of 4-iodoanisole at 400 nm.



9. SPECTRA AND ANALYSES

N.M.R. spectra of 2-iodo-4-nitroanisole and 4-iodo-2-nitroanisole

The spectra of these two isomers were identified by examination of the peaks associated with the 5- and 6-protons, the signal due to these protons being lower τ value for 2-iodo-4-nitroanisole. The spectra were measured on a Perkin Elmer R10.

N.M.R. spectrum of the product of nitrodeiodination of 3-iodoanisole

This compound was identified as 3,6-di-iodo-4-nitroanisole by the n.m.r. spectrum, measured on a Varian HA 100, which showed a singlet at 6.0 τ due to the methoxy protons and two singlets at 1.78 τ and 2.21 τ due to the aromatic protons. The ratio of methoxy protons to aromatic protons was found to be 3:2 by integration of the spectrum.

N.M.R. spectra of 2-phenylthiophen and deuteriated 2-phenylthiophen

Analysis of the integrated spectrum of the deuteriated 2-phenylthiophen, measured on a Varian HA 100, showed deuterium present in the 5-position in the ratio of at least 10:1.

Mass spectrum of product of nitrodeiodination of 3-iodoanisole

The spectrum, measured on an A.E.I. MS 902, showed a molecular ion peak at 405 which is the molecular weight of 3,6-di-iodo-4-nitroanisole.

Infrared spectra

All spectra were measured on a Perkin Elmer 257 infrared spectrophotometer.

Ultraviolet and visible spectra

Full range scans were carried out on a Unicam SP800 and kinetic runs were carried out on, either, a Unicam SP700 or a Unicam SP500

with a SP505 programme controller and a SP22 chart recorder.

Analyses

All analyses for carbon, hydrogen and nitrogen were carried out on a Perkin Elmer PE240. Analyses for iodine were carried out by F.B. Strauss, Oxford.

APPENDIX 1

Investigation of the anomalously high rate of nitration of iodobenzene

When the partial rate factors for the nitration of fluoro-, chloro-, bromo-, and iodobenzene[165,174] are examined, it is found that the order of reactivity for the 4-position is F ≈ I > Cl > Br and each is deactivated relative to benzene. Apart from the position of iodine, the order is that expected for conjugative electron-release, since conjugative interaction should be strongest when the two overlapping orbitals are of approximately the same size[175]. It has been suggested[176] that the unusual result for 4-iodobenzene might be due to a side-reaction such as nitrodeiodination. Bird and Ingold[177] were unable to obtain consistent values for the relative rates of nitration of iodobenzene and benzene, the former sometimes reacting faster than the latter, and their average value for this ratio of 0.18 may be in error. Roberts et al.[165] in more recent work obtained values, which differed with solvent, of 0.13 in nitromethane and 0.22 in acetic anhydride.

It was decided, therefore, to carry out some preliminary investigations as to the involvement of nitrodeiodination in the nitration of iodobenzene. There are two possibilities which could complicate the measurement of partial rate factors. One is that some of the nitration product, 1-iodo-4-nitrobenzene, might be formed by the intermediacy of 1,4-di-iodobenzene, by nitrodeiodination. The 1,4-di-iodobenzene would be formed in a way analogous to the formation of 2,4-di-iodoanisole in the nitrodeiodination of 4-iodoanisole. An experiment was carried out to investigate this possibility. 1,4-Di-iodobenzene was nitrated under conditions identical to those used by Roberts et al.[165]. It was found that, after 22 h, 1-iodo-4-nitrobenzene could be isolated from the reaction products in 45% yield, indicating

that 1,4-di-iodobenzene deiodinates fairly readily, although the reaction time was considerably longer than that used in the determination of relative rate factors. The second possibility is that the iodine released by the nitrodeiodination of iodobenzene attacks the benzene which is present as the reference substrate and is, in fact, the most reactive substrate present. This was checked by nitrating iodobenzene, under the same conditions as above, in the presence of [^{14}C]-benzene. The products of the reaction were separated and tested for radioactivity. Both the iodobenzene and 1-iodo-4-nitrobenzene were found to be inactive while the nitrobenzene was active indicating that the only reaction that benzene had undergone was nitrodeprotonation.

A further experiment was carried out which checked the likelihood of both the above possibilities. It is a necessary consequence of both the schemes that nitrobenzene be found in the products of the nitration of iodobenzene, since the first step in both is nitrodeiodination of this compound, and iodination of nitrobenzene would result in the formation of 1-iodo-3-nitrobenzene rather than 1-iodo-4-nitrobenzene. Therefore the nitration was carried out using [^{14}C]-iodobenzene and unlabelled nitrobenzene was added to the quenched reaction for subsequent retrieval and examination for radioactivity. The results of this experiment indicated that only about 5% of the iodobenzene was converted to nitrobenzene.

It seems, therefore, that the anomalous values for the relative rate of nitration of iodobenzene are unlikely to be due to nitrodeiodination but rather more likely to be due to electronic effects as discussed by Roberts[165].

APPENDIX 2

Investigation of the nitration of iodomesitylene in the presence and absence of sodium nitrite.

Recently a paper has been published[112] that reports the nitration of several iodo-compounds including iodomesitylene, and it is reported that nitrodeiodination occurs resulting, in the stated case, in the formation of nitromesitylene. Further, this work indicates that the species responsible for this reaction is NO_2^+ rather than a nitrosating species. This conclusion is arrived at chiefly by the fact that the addition of urea, which removes nitrous acid, has no noticeable effect on the ratio of nitrodeprotonation and nitrodeiodination products. The efficiency of urea in removing nitrous acid has been discussed earlier in this thesis in connection with ipso factors. It is unlikely that urea removes the last traces of nitrous acid and since the reactants used were pure it seems unlikely that there would be anything but a trace of nitrous acid present under these conditions, and so the situation would be little changed by the addition of urea. It is noticeable that in these experiments the reaction time is relatively long and the yield of the nitrodeiodination product is low.

The obvious experiment that these workers did not carry out is to add nitrous acid to the reaction solution and determine whether this has any effect on the reaction, this would be a more unambiguous proof as to the involvement of nitrosation. It was decided, therefore to carry out this reaction under identical conditions to those used in the original work, adding sodium nitrite, a source of nitrous acid, to one system and urea to another. G.L.C. analysis of the products of each of these reactions indicated that as much as fifteen times more nitromesitylene was obtained in the presence of

sodium nitrite than in the presence of urea. It seems, then, that although the reaction takes place in the presence of urea, whether by attack by NO_2^+ or by nitrosation that the urea cannot prevent, the reaction is greatly enhanced by the presence of nitrous acid, and so nitrosation is significant in this reaction.

APPENDIX 3

Integration of the rate equation for aromatic iodination

The rate equation for the disappearance of iodine (I_2) is,

$$\frac{-d[I_2]}{dt} = k(obs.)[I_2]^{\frac{1}{2}}$$

rearrangement and integration gives,

$$2[I_2]^{\frac{1}{2}} = -k(obs.)t + \text{constant}$$

and the slope of a plot of $[I_2]^{\frac{1}{2}}$ against time, t, is k(obs.)/2.

APPENDIX 4

The explosive properties of nitric acid, acetic anhydride mixtures

A mixture of nitric acid and acetic anhydride is often used as an aromatic nitrating agent, but it is not always realised how dangerous a mixture this can be. Experiments were carried out by Brown and Watt[178], investigating the explosive properties of these mixtures, and the following observations were made:

Using 97% nitric acid and acetic anhydrode, mixtures below 50% w/w did not detonate while mixtures above this composition did. The upper limit for detonation was not determined but it was suggested to be about 85% nitric acid.

Therefore the following conditions should be obeyed when making up these mixtures:

For mixtures whose final composition is below the lower limit for detonation, nitric acid should be added to acetic anhydride.

For mixtures whose final composition is above the upper limit for detonation, acetic anhydride should be added to nitric acid.

Mixtures whose composition is between the two limits should not be used.

In view of the differing densities of nitric acid and acetic anhydride it is useful to restate these limits in terms of volumes:

Lower limit for detonation is about 40% v/v nitric acid.

Upper limit for detonation is about 80% v/v nitric acid.

Dingle and Pryde[179] endorsed this warning and stated that even mixtures below 50% w/w are hazardous, especially if small quantities of water or mineral acid are added to the mixture, the result being an uncontrollable fume-off. Also, they found that aged mixtures even at these low concentrations were far more likely

to detonate at room temperature than freshly prepared solutions, and hot solutions are even more hazardous. To combat this hazard they suggested the addition of 50% acetic acid to increase the heat capacity of the system, which had little effect on yields but greatly increased safety.

APPENDIX 5

Computational aspects

Two computer programmes were written to aid calculations arising from the experimental work for use on the IBM 360/44 computer at the Computational Science Department at St. Andrews.

Programme APRADC

This programme was written to deal with the data from radio-isotopic dilution experiments where two products are formed simultaneously from the same substrate. The ratio of the two products and the extent of reaction is calculated. This is basically a simple calculation if only the quantities of added compound are considered and the quantity of product formed from the reaction is ignored. This latter quantity is not normally neglible and the advantage of this programme is that during the calculation the amount of each product, formed in reaction, can be determined, added to the amount of the particular compound added and the calculation performed again with these new values. This would be a tedious process if done by hand: but this programme enables the calculation to be carried out several times until successive iterations agree to the fourth decimal place.

Input data

Card 1. The weight of each product added to the reaction mixture, then the weight of each product counted, and then the count due to each of these weights, all written in F10.0 format.

Card 2. The weight of substrate originally present, then the weight of substrate counted and the count due to that weight, and then the molecular weights of the substrate and two products, all in F10.0 format.

Example. This is the data from the nitrodeiodination of 4-iodoanisole, stopping the reaction after 35s, and adding 2,4-di-iodoanisole and 4-nitroanisole.

3.0047	3.0037	0.0107	0.0044	530.0	235.0
0.4992	0.0065	5125.0	234.0	360.0	153.0

Output data.

The input values are reproduced, the values obtained in each iteration are listed and the percentage of each product and percentage of reaction which has taken place are displayed.

For the given exam ple, these last three values are 49.5% 2,4-di-iodoanisole, 50.5% 4-nitroanisole and 84.5% reaction.

Programme APKINE

When large numbers of kinetic runs are performed it becomes tedious to work out the rate constants for each one by hand. This programme was written to eliminate this tedium and could be used from a teletype situated near the spectrometers.

The programme was written to deal with kinetics of the first and half-order and was designed especially for use with the spectrometer used for kinetic studies, but options exist to make the programme suitable for more general use. In the programme there are several sections and each is described briefly below.

Main Programme

This section basically reads the input data, sets up the conversion factors and writes the output data.

Subroutine Rate

This section calculates the rate constants for first or half-order kinetics, as required.

Subroutine Alesq

This section is a least squares programme. In addition, after calculating the original slope of from the data, the worst point is eliminated and the calculation performed again. This process is repeated until successive slopes agree to within3% or until a third of the points have been eliminated when a message is given that the slopes do not coverge within the given number of iterations. The linear correlation is also calculated.

Subroutine Pltt

This section processes the data so that it can be plotted by the computer on print-out paper. Points are plotted for experimental values theoretical values obtained from the least-squares analysis and the case where these two values are coincident.

Input data

Card 1. If graphs are required write YES if not write NO.

Card 2. The number of sets of data to be processed as an integer, the order of the reaction, the value of the extinction coefficient (write 0.0 if first-order) as decimal numbers.

Card 3. The run number, the number of readings for that run and the relevant chart speed factor as integers.
Speed factors, for motor position A, F = 1; M = 2, S = 3;
for motor position B, F = 4; M = 5; S = 6.
(If a different chart recorder is used write 7 and the number of seconds per unit on the chart paper in F10.0 format).

Card 4. The value of optical density at infinite time, then the interval between the time values if constant as decimal numbers. (If this interval is not constant, write 0.0 and the

appropriate values on the next card as decimal numbers).

Card 5. The values of optical density at time, t, as decimal numbers. The next run can be written out as from card 3, starting with a new card.

Unless otherwise stated the above data is written in free format, the only condition being that successive numbers on a card be separated by at least one space.

Example The data is from the iodination of thiophen.

NO

1 0.5 768.7

372 14 6

0.28 1.0

.984 .860 .742 .631 .527 .434 .353 .277 .217 .163 .129 .088

.064 .047

Output data

The run number and order of the reaction are printed above a table which lists the time and optical density values, the experimental and theoretical conversion for the graph and the difference between these two values.

Then the linear correlation for the graph used to obtain the rate constant is displayed followed by the points not used in this graph, then distribution of the points used, then the gradient and intercept of the graph, the average difference between the experimental and theoretical conversion values and finally the rate constant calculated from the original data followed by the final rate constant.

```
C       PROGRAMME APRADC
C
C       CALCULATION OF THE RATIO OF TWO PRODUCTS FORMED SIMULTANEOUSLY
C                       FROM THE SAME SUBSTRATE
C
      DIMENSION WAD(2),WCON(2),CON(2),WID(2)
      READ(5,100)WAD,WCON,CON,XORO,WXC,XCON,XMOL,AMOL,BMOL
      AOLD=0.0
      BOLD=0.0
      FOLD=0.0
      F=1.0
      I=0
      WID(1)=WAD(1)
      WID(2)=WAD(2)
      WRITE(6,400)WAD,WCON,CON,XORO,WXC,XCON,XMOL,AMOL,BMOL
      WRITE(6,700)
    2 X=CON(1)*WCON(2)*WID(1)/(CON(2)*WCON(1)*WID(2))
      I=I+1
      WRITE(6,500)X
      BNEW=1.0/(X+1.0)
      ANEW=1.0-BNEW
      F=WXC*((CON(1)*WID(1)/WCON(1))+(CON(2)*WID(2)/WCON(2)
     1))/(XCON*XORO)
      TA=XORO*F*AMOL*ANEW/XMOL
      TB=XORO*F*BMOL*BNEW/XMOL
      WRITE(6,600)TA,TB
      WRITE(6,800)ANEW,BNEW,F
      IF(ABS(ANEW-AOLD).LE.0.0001)GO TO 9
      AOLD=ANEW
      BOLD=BNEW
      FOLD=FNEW
      WID(1)=WAD(1)+TA
      WID(2)=WAD(2)+TB
      IF(I.EQ.10)GO TO 9
      GOTO2
```

```
  9 CONTINUE
    PCA=ANEW*100.0
    PCB=BNEW*100.0
    PCF=F*100.0
    WRITE(6,200) PCA,PCB,PCF
100 FORMAT(6F10.0)
200 FORMAT('0','PERCENT A FORMED =',F6.2,/,'0','PERCENT B FORMED =',F6
   1.2,/,'0','PERCENT REACTION =',F6.2)
300 FORMAT(' ',2X,F8.4,4X,F6.4,4X,F8.4)
400 FORMAT(' ',6F10.4)
500 FORMAT(' ',F10.4)
600 FORMAT(' ',10X,2F10.4)
700 FORMAT('0',5X,'X',9X,'TA',8X,'TB',7X,'ANEW',6X,'BNEW',7X,'F')
800 FORMAT(' ',30X,3F10.4)
    STOP
    END
```

```
C      PROGRAMME APKINE
C
C      FIRST AND HALF ORDER KINETICS PROGRAMME
C
C      MAIN PROGRAMME
C
       COMMON/ALL/ N
       COMMON/MRA/ SLOPE
       COMMON/MR/ ORDER,EP,C,CKOBS,AKOBS,ODF,ODT(20),T(20)
       COMMON/MA/ L,LL,D,B,AVDIF,AX(20),AY(20),AC(20),ADIF(20),
      1PLOT(20),PTNO(6)
       INTEGER S,E,GR,PLOT,A1/'NO'/
       READ(5,200)GR
       CALL IN2 (5,M,ORDER,EP)
       DO 19 E=1,M
       CALL IN2 (5,J,N,S)
       JN=N
       GO TO(9,10,11,12,13,14,15),S
    9  C=21.43
       GO TO 16
   10  C=42.86
       GO TO 16
   11  C=85.72
       GO TO 16
   12  C=30.0
       GO TO 16
   13  C=60.0
       GO TO 16
   14  C=120.0
       GO TO 16
   15  READ(5,900)C
   16  CONTINUE
       CALL IN2 (5,ODF,Z)
       IF(Z.GT.0.0)GO TO 18
       CALL IN1 (5,T,N)
```

```
      GO TO 17
   18 CONTINUE
      T(1)=0.0
      NN=N-1
      DO 17 I=1,NN
      T(I+1)=T(I)+Z
   17 CONTINUE
      CALL IN1 (5,ODT,N)
      LL=0
      CALL RATE
      WRITE(6,150)J,ORDER
      WRITE(6,450)
      DO 21 I=1,JN
      AY(I)=AY(I)/2.3026
      ADIF(I)=ADIF(I)/2.3026
   21 AC(I)=AC(I)/2.3026
      SLOPE=SLOPE/2.3026
      B=B/2.3026
      AVDIF=AVDIF/2.3026
      WRITE(6,350)(T(I),AX(I),ODT(I),AY(I),AC(I),ADIF(I),I=1,JN)
      IF(LL.EQ.1)GO TO 19
      WRITE(6,550)D
      WRITE(6,750)(PTNO(I),I=1,L)
      WRITE(6,250)(PLOT(I),I=1,N)
      WRITE(6,400)SLOPE,B,AVDIF,CKOBS,AKOBS
      IF(GR.EQ.A1)GO TO 19
      CALL PLTT
      IF(ORDER.EQ.0.5)GO TO 20
      WRITE(6,950)
      GO TO 19
   20 WRITE(6,700)
   19 CONTINUE
  150 FORMAT('1',18X,'RUN ',I3,16X,'TEST ORDER ',F3.1)
  200 FORMAT(A3)
  250 FORMAT('0','DISTRIBUTION OF POINTS;',/,20I4)
```

```
  350 FORMAT(3X,F5.2,4X,F8.2,5X,F6.3,5X,F7.4,6X,F7.4, 6X,F7.4)
  400 FORMAT('0','GRADIENT = ',F8.5,/,'0', 'INTERCEPT = ',F8.5,/,'0',
     1'AV.DIFFERENCE = ',F7.4,/,'0','ORIGINAL K OBS =',E11.4,' UNITS',
     2/,'0','   FINAL K OBS =',E11.4,' UNITS')
  450 FORMAT('0',1X,'TIME(SQ)',3X,'TIME(SEC)',3X,'OPTICAL',3X,'CONVERSIO
     1N',3X,'CALCULATED',3X,'DIFFERENCE',/,25X,'DENSITY',16X,'CONVERSION
     2')
  550 FORMAT('0','LINEAR CORRELATION = ',F7.4)
  700 FORMAT('0',26X,' HALF ORDER PLOT')
  750 FORMAT('0','POINTS NOT USED FOR FINAL CALCULATION;',/,6F9.2)
  900 FORMAT(F10.0)
  950 FORMAT('0',26X,'FIRST ORDER PLOT')
      STOP
      END
C
C     THIS SUBPROGRAMME CALCULATES THE RATE DATA
C
      SUBROUTINE RATE
      COMMON/ALL/ N
      COMMON/MRA/ SLOPE
      COMMON/RAP/ X(20),Y(20)
      COMMON/RA/ CSLOPE
      COMMON/MR/ ORDER,EP,C,CKOBS,AKOBS,ODF,ODT(20),T(20)
      IF (ORDER.EQ.0.5)GO TO 2
      DO 1 I=1,N
      A=ODF-ODT(I)
      Y(I)=ALOG(A)
      X(I)=T(I)*C
    1 CONTINUE
      CALL ALESQ
      AKOBS=(ABS(SLOPE))
      CKOBS=ABS(CSLOPE)
      GO TO 4
    2 DO 3 I=1,N
      Y(I)=SQRT(ABS(ODT(I)-ODF))
```

```
      X(I)=T(I)*C
    3 CONTINUE
      CALL ALESQ
      AKOBS=ABS(SLOPE*2.0)/SQRT(EP)
      CKOBS=ABS(CSLOPE*2.)/SQRT(EP)
    4 CONTINUE
      RETURN
      END
C
C     THIS IS A LEAST SQUARES SUBPROGRAMME
C
      SUBROUTINE ALESQ
      COMMON/ALL/ N
      COMMON/MRA/ SLOPE
      COMMON/RAP/ X(20),Y(20)
      COMMON/RA/ CSLOPE
      COMMON/MA/ L,LL,D,B,AVDIF,AX(20),AY(20),AC(20),ADIF(20),
     1PLOT(20),PTNO(6)
      COMMON/AP/ F(20)
      DIMENSION TEST(20),DIF(20)
      INTEGER PLOT
      IK=0
      JP=N
      JA=N/3
      ASLOPE=0.
    8 CONTINUE
      N=JP
      SUMX=0.0
      SUMY=0.0
      SUMXY=0.0
      SUMXX=0.0
      SUMYY=0.0
      TDIF=0.0
      DO 2 I=1,N
      SUMX=SUMX+X(I)
```

```
      SUMY=SUMY+Y(I)
      SUMXY=X(I)*Y(I)+SUMXY
      SUMXX=X(I)*X(I)+SUMXX
      SUMYY=Y(I)*Y(I)+SUMYY
    2 CONTINUE
      G=N
      DENOM=SUMX*SUMX-G*SUMXX
      DENON=SUMY*SUMY-G*SUMYY
      SLOPE=(SUMX*SUMY-G*SUMXY)/DENOM
      B=(SUMX*SUMXY-SUMY*SUMXX)/DENOM
      D=ABS((G*SUMXY-SUMX*SUMY)/SQRT(DENOM*DENON))
      DO 3 I=1,N
      F(I)=SLOPE*X(I)+B
      DIF(I)=Y(I)-F(I)
      TDIF=TDIF+(ABS(DIF(I)))
      IF(IK.GT.0)GO TO 3
      AX(I)=X(I)
      AY(I)=Y(I)
      AC(I)=F(I)
      ADIF(I)=DIF(I)
    3 CONTINUE
      AVDIF=TDIF/G
      IF(IK.EQ.0)CSLOPE=SLOPE
      AP=0.0
      DO   1 I=1,JP
      TEST(I)=(DIF(I)/AVDIF)*10.0
      PLOT(I)=TEST(I)
      IF( ABS(TEST(I)).LT.AP)GO TO 1
      AP=ABS(TEST(I))
      IP=I
    1 CONTINUE
      IF(ABS(SLOPE-ASLOPE).LE.ABS(SLOPE)/30.)GO TO 6
      IF(IK.GE.JA)GO TO 5
      JP=JP-1
      L=IK+1
```

```
      PTNO(L)=X(IP)
      DO 7 J=IP,JP
      X(J)=X(J+1)
    7 Y(J)=Y(J+1)
      IK=L
      ASLOPE=SLOPE
      GO TO 8
    5 IA=JA+1
      WRITE(6,100) IA
      LL=1
    6 CONTINUE
  100 FORMAT('0','SLOPE DOES NOT CONVERGE SUFFICIENTLY WITHIN ',I2,' ITE
     1RATIONS')
      RETURN
      END
C
C     THIS SUBROUTINE PLOTS THE RESULTS FROM THE MAIN PROGRAMME
C
      SUBROUTINE PLTT
      COMMON/ALL/ N
      COMMON/AP/ F(20)
      COMMON/RAP/ X(20),Y(20)
      DIMENSION IPL(65),JPL(65),KPL(65),LPL(65)
      INTEGER IB/' '/,IF/'C'/,IY/'X'/,IEQ/'*'/
      FMAX=-.1E25
      YMAX=-1.E25
      XMAX=-1.E25
      FMIN=1.E25
      YMIN=1.E25
      XMIN=1.E25
      DO 15 I=1,N
      IF(F(I)-FMAX.LE.0.)GO TO 10
      FMAX=F(I)
   10 IF(F(I)-FMIN.GT.0.)GO TO 11
```

```
      FMIN=F(I)
   11 IF (Y(I)-YMAX.LE.0.)GO TO 12
      YMAX=Y(I)
   12 IF (Y(I)-YMIN.GE.0.)GO TO 13
      YMIN=Y(I)
   13 IF(X(I)-XMAX.LE.0.)GO TO 14
      XMAX=X(I)
   14 IF(X(I)-XMIN.GT.0.)GO TO 15
      XMIN=X(I)
   15 CONTINUE
      XINC=(XMAX-XMIN)/64.
      GMAX=YMAX
      IF(GMAX-FMAX.GT.0.)GO TO 16
      GMAX=FMAX
   16 CONTINUE
      GMIN=FMIN
      IF(GMIN-YMIN.LE.0.)GO TO 17
      GMIN=YMIN
   17 CONTINUE
      GINC=(GMAX-GMIN)/34.
      WRITE (6,100)XMIN,XMAX,XINC,GMAX,GMIN,GINC
      WRITE(6,200)
      IF(XINC*GINC.EQ.0.)GO TO 40
      DO 19 I=1,65
      IPL(I)=0
      JPL(I)=0
      KPL(I)=0
   19 CONTINUE
      DO 20 I=1,N
      IK=(Y(I)-GMIN)/GINC
      II=35-IK
      IPL(I)=II
      IK=(F(I)-GMIN)/GINC
      II=35-IK
      JPL(I)=II
      IK=(X(I)-XMIN)/XINC
```

```
      II=IK+1
      KPL(I)=II
   20 CONTINUE
      M=0
      DO 40 I=1,35
      M=M+1
      DO 23 K=1,65
      LPL(K)=0
   23 CONTINUE
      DO 25 J=1,N
      IF(IPL(J)-I.NE.0) GO TO 25
      JJ=KPL(J)
      LPL(JJ)=1
   25 CONTINUE
      DO 30 J=1,N
      IF(JPL(J)-I.NE.0) GO TO 30
      JJ=KPL(J)
      IF (LPL(JJ)-2.GE.0) GO TO 30
      LPL(JJ)=LPL(JJ)+2
   30 CONTINUE
      DO 36 J=1,65
      IF(LPL(J).NE.0) GO TO 32
      LPL(J)=IB
      GO TO 36
   32 IF(LPL(J)-2) 33,34,35
   33 LPL(J)=IY
      GO TO 36
   34 LPL(J)=IF
      GO TO 36
   35 LPL(J)=IEQ
   36 CONTINUE
      IF(M-5.EQ.0)GO TO 38
      WRITE(6,300) (LPL(J),J=1,65 )
      GO TO 40
   38 WRITE(6,400) (LPL(J),J=1,65 )
```

```
      M=0
   40 CONTINUE
      WRITE(6,200)
  100 FORMAT('1','HORIZONTAL IS TIME,VAL.AT LEFT=',F5.2,'VAL.AT RIGHT=',
     1F8.2,' INC.=',F6.2,/'VERTICAL IS CONVERSION,VAL.AT TOP=',F5.2,' VA
     2L.AT BOTTOM=',F5.2,' INC.=',F5.2,/,'X IS EXP.VAL. O IS CALC.VAL.AN
     3D * IS EQUAL EXP.AND CALC.VALS.',/,' ')
  200 FORMAT(' ',1X,'A+----+----+----+----+----+----+----+----+----+----
     1+----+----+----A')
  300 FORMAT (2X,'|',65A1,'|')
  400 FORMAT (2X,'+',65A1,'+')
      RETURN
      END
```

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